PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF
THE EDITORIAL COMMITTEE

HONORARY EDITORS:
R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH

SESSION 1943-44

NOVEMBER, 1943—OCTOBER, 1944

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

JOINT DISCUSSIONS

CONTENTS

SECTION OF ANÆSTHETICS

CONTENTS .

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE·

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   *SESSION 1943-44*

SECTION FOR THE STUDY OF DISEASE IN CHILDREN

OFFICERS:

President—ERIC A. CROOK, M.Ch.

Vice-Presidents—A. G. MAITLAND-JONES, O.B.E., M.D.; DONALD PATERSON, M.D.;
Surg. Rear-Admiral C. P. G. WAKELEY, C.B.

Hon. Secretaries—A. W. FRANKLIN, F.R.C.P.; G. H. NEWNS, M.D.

Other Members of Council—DENIS J. BROWNE, F.R.C.S.; BERYL CORNER, M.D.; DONALD
COURT, M.R.C.P.; ELAINE FIELD, M.D.; G. H. MACNAB, F.R.C.S.; D. W. C.
NORTHFIELD, M.S.; J. N. O'REILLY, D.M.; C. T. POTTER, M.D.; URSULA SHELLEY,
M.D.; A. G. WATKINS, M.B.; H. W. S. WRIGHT, M.S.

Representative on Library Committee—Wing Cdr. R. W. B. ELLIS, R.A.F.V.R.

Representative on Editorial Committee—A. G. SIGNY, M.B.

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   *SESSION* 1943-44

CLINICAL SECTION

OFFICERS:

President—J. D. ROLLESTON, M.D.

Vice-Presidents—E. A. COCKAYNE, D.M.: ERIC A. CROOK, M.Ch.; LEONARD FINDLAY, M.D.; G. H. MACNAB, F.R.C.S.: S. P. MEADOWS, M.D.; J. E. H. ROBERTS, O.B.E., F.R.C.S.

Hon. Secretaries—KENNETH HERITAGE, F.R.C.S.; WILFRED STOKES, M.D.

Other Members of Council—Lt.-Col. H. J. B. ATKINS, R.A.M.C.: Surg. Lt.-Cdr. E. M. BUZZARD, R.N.V.R.; Sir MAURICE CASSIDY, K.C.V.O., M.D.; HUGH GAINSBOROUGH, M.D.; P. E. T. HANCOCK, M.R.C.P.; R. VAUGHAN HUDSON, F.R.C.S.; EVAN JONES, F.R.C.P.; C. E. NEWMAN, M.D.: Flight Lt. B. G. PARSONS-SMITH, R.A.F.V.R.; B. T. PARSONS-SMITH, M.D.; PHILIP TURNER, M.S.; A. DICKSON WRIGHT, M.S.

Representative on Library Committee—NEILL HOBHOUSE, M.D.

Representative on Editorial Committee—B. T. PARSONS-SMITH, M.D.

CONTENTS

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   *SESSION 1943-44*

SECTION OF COMPARATIVE MEDICINE

OFFICERS:

President—J. T. EDWARDS, M.R.C.V.S.

Immediate Past President—Sir ALEXANDER FLEMING, F.R.C.S., F.R.S.

Vice-Presidents—C. H. ANDREWES, M.D., F.R.S. ; Sir JOSEPH ARKWRIGHT, M.D., F.R.S. ; S. P. BEDSON, M.D., F.R.S. ; G. R. CAMERON, F.R.C.P. ; Major C. DAVENPORT, O.B.E., R.A.V.C. ; Sir JOHN LEDINGHAM, C.M.G., M.B., F.R.S. ; H. W. STEELE-BODGER, M.R.C.V.S.

Hon. Secretaries—C. L. OAKLEY, M.D. ; R. LOVELL, M.R.C.V.S.

Other Members of Council—V. D. ALLISON, M.D. ; W. H. ANDREWS, M.R.C.V.S. ; T. J. BOSWORTH, M.R.C.V.S. ; THOMAS DALLING, M.R.C.V.S. ; A. W. DOWNIE, M.D. ; G. M. FINDLAY, C.B.E., M.D. ; J. FRANCIS, M.R.C.V.S. ; R. E. GLOVER, F.R.C.V.S. ; H. T. MATTHEWS, F.R.C.V.S. ; H. J. PARISH, M.D. ; W. A. POOL, M.R.C.V.S. ; R. W. SCARFF, M.B. ; A. W. STABLEFORTH, M.R.C.V.S. ; W. G. SUTTON, M.Sc. ; E. G. WHITE, M.R.C.V.S. ; A. N. WORDEN, M.R.C.V.S.

Representative on Library Committee—W. A. POOL, M.R.C.V.S.

Representative on Editorial Committee—R. LOVELL, M.R.C.V.S.

DISCUSSION ON CASES TREATED BY PENICILLIN

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

VOLUME THE THIRTY-SEVENTH.   *SESSION* 1943-44

SECTION OF COMPARATIVE MEDICINE

DISCUSSION ON CASES TREATED BY PENICILLIN

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   SESSION 1943-44

SECTION OF COMPARATIVE MEDICINE

OFFICERS:

President—J. T. EDWARDS, M.R.C.V.S.

Immediate Past President—Sir ALEXANDER FLEMING, F.R.C.S., F.R.S.

Vice-Presidents—C. H. ANDREWES, M.D., F.R.S. ; Sir JOSEPH ARKWRIGHT, M.D., F.R.S. ;
S. P. BEDSON, M.D., F.R.S. ; G. R. CAMERON, F.R.C.P. ; Major C. DAVENPORT,
O.B.E., R.A.V.C. ; Sir JOHN LEDINGHAM, C.M.G., M.B., F.R.S. ; H. W. STEELE-
BODGER, M.R.C.V.S.

Hon. Secretaries—C. L. OAKLEY, M.D. ; R. LOVELL, M.R.C.V.S.

Other Members of Council—V. D. ALLISON, M.D. ; W. H. ANDREWS, M.R.C.V.S. ; T. J.
BOSWORTH, M.R.C.V.S. ; THOMAS DALLING, M.R.C.V.S. ; A. W. DOWNIE, M.D. ;
G. M. FINDLAY, C.B.E., M.D. ; J. FRANCIS, M.R.C.V.S. ; R. E. GLOVER, F.R.C.V.S. ;
H. T. MATTHEWS, F.R.C.V.S. ; H. J. PARISH, M.D. ; W. A. POOL, M.R.C.V.S. ;
R. W. SCARFF, M.B. ; A. W. STABLEFORTH, M.R.C.V.S. ; W. G. SUTTON, M.Sc. ;
E. G. WHITE, M.R.C.V.S. ; A. N. WORDEN, M.R.C.V.S.

Representative on Library Committee—W. A. POOL, M.R.C.V.S.

Representative on Editorial Committee—R. LOVELL, M.R.C.V.S.

April 14, 1944

DISCUSSION ON CASES TREATED BY PENICILLIN

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF COMPARATIVE MEDICINE

OFFICERS :

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF DERMATOLOGY

OFFICERS:

CONTENTS

SECTION OF DERMATOLOGY WITH
SECTION OF EPIDEMIOLOGY AND STATE MEDICINE
(JOINT DISCUSSION No. 2)

December 16, 1943

THE ORGANIZATION OF THE TREATMENT OF LUPUS VULGARIS

Dr. F. S. AIREY (pp. 291 and 299), Sir HENRY GAUVAIN (p. 292), Dr. ARTHUR BURROWS (pp. 293 and 300), Dr. F. R. G. HEAF (pp. 294 and 300), Dr. HENRY MACCORMAC (p. 296), Major W. J. O'DONOVAN (p. 296), Dr. A. M. H. GRAY (p. 297), Dr. J. A. H. BRINCKER (p. 298), Dr. J. T. INGRAM (p. 298), Surgeon Lieutenant-Commander H. R. VICKERS (p. 298), Dr. R. T. BRAIN (p. 298), Sir WELDON DALRYMPLE-CHAMPNEYS (p. 299), Dr. D. E. MACRAE (p. 300).

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF EPIDEMIOLOGY AND STATE MEDICINE

SECTION OF EXPERIMENTAL MEDICINE AND THERAPEUTICS

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

VOLUME THE THIRTY-SEVENTH.   *SESSION 1943-44*

SECTION OF EXPERIMENTAL MEDICINE AND THERAPEUTICS

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

VOLUME THE THIRTY-SEVENTH.   *SESSION* 1943-44

SECTION OF THE HISTORY OF MEDICINE

OFFICERS :

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF THE HISTORY OF MEDICINE

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF LARYNGOLOGY

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF MEDICINE

CONTENTS

SECTION OF NEUROLOGY

OFFICERS :

CONTENTS

SECTION OF OBSTETRICS & GYNÆCOLOGY

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   *SESSION 1943-44*

SECTION OF ODONTOLOGY

OFFICERS:

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF OPHTHALMOLOGY

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

VOLUME THE THIRTY-SEVENTH.   *SESSION* 1943-44

SECTION OF ORTHOPÆDICS

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

SECTION OF OTOLOGY

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF OTOLOGY

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF PHYSICAL MEDICINE

OFFICERS:

President—P. BAUWENS, M.R.C.S., L.R.C.P.

Immediate Past President—Major G. D. KERSLEY, R.A.M.C.

Vice-Presidents—LEONARD BOYS, M.B.; C. W. BUCKLEY, M.D.; F. I. DAWSON, F.R.C.S.Ed.; A. R. NELIGAN, M.D.; Major J. W. T. PATTERSON, R.A.M.C.; DRURY PENNINGTON, M.B.

Hon. Secretaries—HUGH BURT, M.R.C.P.; FRANCIS BACH, M.D.

Other Members of Council—W. BEAUMONT; FRANK COOKSEY, M.D.; Lieut.-Col. W. S. C. COPEMAN, R.A.M.C.; E. J. CRISP, M.B.; Lieut.-Col. L. C. HILL, R.A.M.C.; G. K. STONE, M.D.; Major H. F. TURNEY, R.A.M.C.

Representative on Library Committee—Sir ROBERT STANTON WOODS, M.D.

Representative on Editorial Committee—M. B. RAY, D.S.O., M.D.

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.   *SESSION 1943-44*

SECTION OF PROCTOLOGY

OFFICERS:

CONTENTS

SECTION OF PHYSICAL MEDICINE WITH SECTION FOR THE
STUDY OF DISEASE IN CHILDREN
(*JOINT DISCUSSION No.* 1)

November 17, 1943

DISCUSSION ON ANTERIOR POLIOMYELITIS

SECTION OF PROCTOLOGY

OFFICERS :

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF PSYCHIATRY

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: R. DAVIES-COLLEY, C.M.G., M.Ch., and MAURICE DAVIDSON, M.D.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE THIRTY-SEVENTH.　　　*SESSION* 1943-44

SECTION OF RADIOLOGY

OFFICERS:

President and Chairman of Council—N. S. FINZI, M.B.

Immediate Past President—F. M. ALLCHIN, M.B.

Vice-Presidents—A. E. BARCLAY, O.B.E., M.D. ; F. CAMPBELL GOLDING, M.B. ; E. DUFF GRAY, M.D. ; B. W. WINDEYER, F.R.C.S.Ed.

Hon. Secretaries—W. M. LEVITT, M.D. ; J. V. SPARKS.

Other Members of Council—S. WHATELY DAVIDSON, M.D. ; H. K. GRAHAM HODGSON, C.V.O. F.R.C.P. ; A. S. JOHNSTONE, F.R.C.S.Ed. ; PETER KERLEY, M.D. ; JOHN B. KING, M.D. ; J. W. McLAREN ; E. E. TALLENT NUTHALL, M.D. ; R. O'DONOGHUE, M.B. ; J. RALSTON PATERSON, M.C., F.R.C.S.Ed. ; Major ERIC SAMUEL, R.A.M.C. ; E. W. H. SHAWCROSS ; Surg. Cdr. A. ROBINSON THOMAS, R.N.V.R. ; E. ROHAN WILLIAMS, M.D.

Representative on Library Committee—F. CAMPBELL GOLDING, M.B.

Representative on Editorial Committee—F. CAMPBELL GOLDING, M.B.

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

SECTION OF SURGERY

CONTENTS

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

VOLUME THE THIRTY-SEVENTH.   *SESSION* 1943-44

SECTION OF UROLOGY

OFFICERS:

CONTENTS

Section of Odontology

President—B. Maxwell Stephens, L.D.S.E.

[*March* 22, 1943]

The Dental Epithelium and its Significance in Tooth Development

By W. Warwick James, O.B.E., F.R.C.S. and A. W. Wellings. D.Sc., M.D.S.

In the present circumstances it is only possible to publish a summary of the paper read before the Section in March with a limited number of illustrations. It is hoped a fuller publication may be possible later.

The Dental Epithelium we have defined as "The Special Epithelium concerned with the development, eruption and fixation of teeth".

It has two chief functions, one the formation of the teeth and the other, the determination and maintenance of their position. It is the latter with which we are concerned in this paper. The former has previously received nearly all the attention of investigators.

The following functions can be attributed to the dental epithelium: (*a*) The production, directly and indirectly, of the dental tissues. (*b*) The determination of the shape of the tooth. (*c*) Fixation of the exact position in which a tooth will develop and the point at which it will erupt. (*d*) The formation of an almost complete epithelial envelope as a capsule enclosing the germ or tooth during the whole process of development, including complete eruption. (*e*) Maintaining connexion between the epithelial envelope and the surface epithelium by means of the connecting dental epithelium.

A factor of much importance when considering the changes occurring in the dental epithelium is the rapidity and extent of its growth.

We found it necessary to extend our investigation to all vertebrates with teeth, for it seemed reasonable to suppose that the process of tooth production is essentially the same throughout. It is only possible to make generalizations which apply to this very wide field.

Source of Material : Stock-animals have been obtained from the laboratories in which we work: The Bland-Sutton Institute of the Middlesex Hospital and the Dental Research Laboratory of Birmingham University, where most of the work has been done during the war. A large number of rare and other specimens has been obtained from the London Zoological Society for more than ten years, and it is upon much of this material that our paper depends. Many friends have procured specimens and serial sections were lent by Dr. Fish (pike) and Mr. Manley (conger eel). Laboratory animals such as frog, kitten and rat were used for precise intervals of age, and for comparison with those less easily procured. It was found necessary to employ the celloidin paraffin method for nearly all specimens. Many sections have been cut which are not good enough for detail, although the dental epithelium is sufficiently well shown to give some indication of its importance. Failure to obtain really good fixation was a frequent difficulty. In the case of the rare animals specimens were often procured only after they had been dead for many hours. Such material is valuable although imperfect. This also applies to our native animals many of which had not been fixed for some hours after death. Fixation by spirit has been most unsatisfactory although material so preserved has been cut when none other has been available. It is obvious that examination of all animals is an impossibility, but selected types at varying ages have been studied, and in each case serial sections were prepared and different staining methods employed (Wellings, 1938).

There appear to be four sites of origin of dental germs from the dental epithelium:
(1) From the surface epithelium. (2) From the sheath epithelium. (3) From a persistent dental lamina. (4) From a non-persistent dental lamina.

(1) Origin from the surface epithelium occurs in some of the superficial teeth of teleostei, e.g. pike (fig. 1). It is described by Harrison (1901) in sphenodon, by Bolk (1912) and Woerdeman (1919) in *Crocodilus porosus*. They are akin to dermal denticles. The initial tooth of a dental unit may be of this nature in some animals, e.g. frog. Röse (1891) described it in Triton.

(2) Origin from the sheath epithelium of a preceding tooth. It occurs in the teleostei, e.g. the garpike, the eel, catfish, pike and mackerel, &c. (figs. 1, 2, 3). It is a method of replacement by successional teeth.

(3) Origin from a persistent dental lamina occurs in the selachii, amphibia and most reptiles. The successional germ arises near the terminal margin (figs. 4, 5, 9).

(4) Origin from a non-persistent dental lamina occurs in marsupials and mammals (fig. 6). It proliferates to produce the connecting dental epithelium, its continuity as

CONTENTS

The Society does not hold itself in any way responsible for the statements made or the views
put forward in the various papers.

epithelium and the surface dental epithelium, are chiefly responsible for the positioning of the tooth, and are aided by the sheath epithelium as the formation of the subcoronal part of the tooth progresses.

(*a*) *The coronal part of the epithelial envelope :* The outline of the epithelial envelope varies at its successive stages and with different types of animals. In the lower forms it roughly corresponds with the shape of the tooth. In the higher forms, where the germs are more deeply situated and a stellate reticulum is often present in the earlier stages, it has a more or less globular outline rendered superficially irregular by proliferating buds and processes on its coronal part (figs. 16, 17, 18).

Deeply situated germs in the lower forms present some of these characteristics. In the wrasse, cichlid (figs. 8 and 11) and others there is marked proliferation of the coronal epithelium, producing the gland-like appearance described by Mummery in *Sargus ovis* to which he ascribed a secretory function.

In polyphyodont animals with a persistent dental lamina (selachii, amphibia and some reptilia) the epithelial envelope is attached to the lamina along which, as the tooth grows, it appears to move until it joins the surface epithelium to form the attachment (fig. 5).

In diphyodont animals in the early stages where the dental lamina is non-persistent, as proliferation progresses the epithelial envelope is connected to the lamina in a manner which varies in complexity, with different teeth and at different stages. Thus the envelope may be attached to the lamina directly, or by a strand of cells at one stage, while at another the two-strand phase described by Bolk (1921) may be seen, and at other stages the connexions may be still more complex as a network (figs. 14, 15, 16, 17 and 18). The detailed arrangement needs further study. It is sufficient at present to direct attention to the fact that the epithelial envelope and the lamina forming the connecting dental epithelium, are not in a static condition.

In crocodilia the enamel organ is of particular interest on account of the importance attached to it by Bolk (1921). In a specimen from a spectacled caiman (*Caiman crocodilus*) (fig. 19) the envelope dips in at its summit to form a depression, similar to an "enamel navel", from which a condensation of cells, an "enamel septum", divides the stellate reticulum in a manner described by him as occurring only in mammals. It would thus seem that the part of his dimeric theory which is based upon the occurrence of these phenomena only in the mammalian enamel organ, is unsound.

Throughout development epithelial projections into the mesoderm are constant and have a definite distribution over the summit of the envelope. They are seen as buds when small, but often with the increasing size of the germ, as longer processes. These are particularly noticeable in mammals (figs. 14, 15, 16, 17, 18).

The relation of the buds and processes of the epithelial envelope to the capillary blood-vessels is very striking. The association is most marked where active proliferation is in progress (figs. 16, 26).

As the crown of the tooth nears completion the cells of the envelope become compressed on to the other remaining cells of the enamel organ to form the epithelial lining of the tooth follicle (fig. 21). The tooth and its epithelial envelope as they increase in size, approach the surface, a movement largely due to the changes in the mesoderm taking place at the unenclosed part of the envelope (the base of the tooth) with lengthening of the root.

The final function of the epithelial envelope is the formation of the epithelial structures over the crown of the tooth and assistance in fixation at its ultimate position (fig. 20).

The character of the mesoderm around the mammalian germ presents constant and special features. It is composed of very delicate fibres which stain but feebly with collagen stains, and some scattered nuclei. Its appearance is so striking that we have called it the "Stellate Mesoderm" on account of its close resemblance to the "stellate reticulum" of the enamel organ for which in fact it may be mistaken. It is so characteristic a feature in the early stages of a developing tooth in mammals, that an approaching germ can be predicted from the appearance of the stellate mesoderm in some sections of a series before the germ itself appears (fig. 26).

(*b*) *Sheath epithelium or sheath of Hertwig :* This is an extension from the coronal margin of the epithelial envelope together with a similar extension from the internal epithelium of the enamel organ. It surrounds the subcoronal part of every tooth whether ankylosed or socketed (figs. 9, 10, 11, 12). In the latter we have called it the Root Sheath Epithelium (figs. 20 and 21).

It has been described in amphibia' by Hertwig (1874); in rodents, ungulates and carnivora by von Brunn (1887, 1891); and by Mummery (1924) and others, also by Tomes (1923) in some detail in human teeth. The presence of special dental epithelial cells is necessary for the formation of dentine, this has long been recognized and has recently been confirmed by the experimental work *in vitro* by Miss Glasstone (1930 and 1938).

In certain lower types of animals a sharp distinction cannot be drawn between the coronal part of the epithelial envelope and the subcoronal part or sheath epithelium,

a lamina being lost at an early stage. This is well shown in figs. 8 and 9 of the paper by Röse (1891) in which his reconstruction models are described.

Once initiated the dental epithelium can be readily placed under headings which define areas with special morphological and functional attributes.

(1) The Epithelial Framework and the Dental Zone. (2) The Dental Unit. (3) The Epithelial Envelope: (a) coronal part; (b) sheath epithelium or subcoronal part. (4) The Dental Lamina and the Connecting Dental Epithelium. (5) The Surface Dental Epithelium.

(1) The Dental Epithelial Framework and Dental Zone

Following initial proliferation from the surface epithelium an extensive production of dental epithelium occurs throughout the tooth-bearing area, with the formation of an epithelial framework composed of surface epithelium connecting a series of units made up of teeth and successional germs. The total area for purposes of description can be called a "Dental Zone". A sufficiently sharp distinction exists between teeth and dermal denticles to define the limit of a zone; in higher types it is easily recognized. Sections through the dental zone show dental epithelium which can be connected together only by examining serial sections, to give a complete picture, as in dog-fish, pike, eel, lizard, snake and man, &c. (figs. 1, 4, 7, 8 show one plane). The connexions seen in one section may be in part continuous or scattered. In the lower forms continuity is readily established in a few sections but in higher forms many of a series may need to be examined (James, 1909).

The dental zone is composed of the surface epithelium connecting a series of units, which correspond in number with each erupted tooth and its successors. Each of these individual groups we have named a dental unit.

The recognition of an epithelial framework indicates a continuity which is maintained between all the dental elements, whatever changes of proliferation, maturity or degeneration the dental epithelium undergoes.

Although the initial changes are seen in the dental epithelium, they are soon followed by the induction of important differential changes in the mesoderm. The resulting mesodermal structures, not only those forming the teeth, must be regarded as belonging to the dental zone.

(2) The Dental Unit

This is an entity in the epithelial framework of the dental zone consisting of an erupted tooth and its successor or successors connected by dental epithelium. In polyphyodont animals the individual tooth and its successors are always connected by dental epithelium forming a chain consisting of a formed tooth, a developing tooth, and one or more following dental germs. A similar arrangement holds in diphyodonts.

No lateral communication occurs between dental units except at the surface (figs. 1 and 7). Where the germs are attached to a persistent dental lamina, this also provides further lateral communication (figs. 5 and 9).

Whether there is a stage of discontinuity in any animal with later reunion of the dental epithelium is extremely doubtful.

The condition in crocodilia is unusual where the replacing tooth germ soon passes into the pulp chamber of the functional tooth in which position its development is completed. In due course as the old tooth becomes cast off, surface continuity of the new tooth is established by the junction of its epithelial envelope with the surface epithelium (fig. 10).

Within the unit continuity is maintained by means of the epithelial envelope, the connecting dental epithelium and the surface dental epithelium.

Successional teeth and germs are grouped by Bolk as "families".

(3) The Epithelial Envelope

An envelope of dental epithelium which encapsules the forming tooth throughout development including attainment of final position, is formed by the outer layer of cells of the enamel organ and is complete, except where the mesodermal tissues of the tooth are being produced at its base. When fully developed it consists of two parts (a) a coronal, and (b) an extension over the subcoronal part of the tooth. Externally it is in contact with the surrounding mesoderm except where it has attachment to the connecting dental epithelium. It is readily recognized in all animals (figs. 8, 10, 11, 12, 13, 20, 21).

As the developing tooth increases in all dimensions so the envelope grows by proliferation of its cells. Provision for increase in depth is made by proliferation of the cells at the base of the enamel organ. This extension of the envelope over the subcoronal part of the tooth constitutes the "sheath epithelium". It is important to realize that the two parts are continuous.

We are of the opinion that the coronal part of the envelope, the connecting dental

is difficulty in establishing the exact attachment. If this is so the great accuracy of the points of eruption would be established.

The recognition of the proliferations of the dental epithelium contradicts the generally accepted view that the dental lamina is lost (figs. 24 and 25). This applies in particular to man where only functionless remnants are said to persist. It certainly does not disappear in the lower forms of animals, and the connexions of its proliferations with the epithelial envelope and the surface dental epithelium constitute the continuity in the higher forms, including man (figs. 24 and 25).

(5) SURFACE DENTAL EPITHELIUM

This is that part of the surface epithelium in a dental zone which undergoes proliferation of its deeper cells. It forms the most superficial part of the connecting dental epithelium.

It may persist from the initial formation of the dental epithelium (fig. 6), but in all animals it occurs as an active proliferation prior to the eruption of a tooth. It can be seen over the erupting teeth of such divergent animals as fishes, amphibia, reptiles and mammals (fig. 21).

The final position of a tooth is established in mammalia by the junction of the epithelial envelope with the surface epithelium (fig. 20).

In the lower forms the loss of surface cells is most marked calling for rapid replacement, and there can be no doubt that this rapidity of waste and repair is an important feature in the movement of the successional teeth to the surface. This aspect of the subject, however, belongs, strictly speaking, to eruption which we have not dealt with except indirectly, in this paper.

SUMMARY

(1) Tooth development in all tooth-bearing animals is essentially the same.

(2) It depends primarily upon the differentiation of certain cells of the surface epithelium of the mouth with potentialities for tooth formation.

(3) The various epithelial structures resulting from the proliferation of these specialized cells constitutes the dental epithelium.

(4) It is convenient to describe four different sites of origin of tooth germs following the initial proliferation:

(*a*) Surface Epithelium. (*b*) Sheath Epithelium. (*c*) Persistent Dental Lamina. (*d*) Non-persistent Dental Lamina.

(5) The initial proliferation determines the position of the developing germ and the point of eruption. The position of successional germs, and their eruption points are also pre-determined at the same time. Thus the original inflection that fixes the position of the minute teeth in the jaws of the newly-hatched crocodile, predetermines the position of the immensely larger teeth of the adult animal.

(6) Emphasis has been laid upon the importance of the dental epithelium in positioning the tooth, directing its path of eruption, establishing union at the surface and fixing it in its functional position.

(7) We have classified the dental epithelium under headings which possess definite morphological and functional features. Thus it forms a "dental epithelial framework" distributed throughout the tooth-bearing areas of the jaws, which in its various manifestations as "surface dental epithelium" the "epithelial envelope" and "connecting dental epithelium" joins up the individual elements of a "dental unit" and finally establishes their relationship both at the surface and with each other. The tooth-bearing region with its accompanying mesodermal structures constitutes the "dental zone."

(8) A dental unit contains all the individual teeth which are produced from one germ centre, and so is applicable to monophyodont, diphyodont and polyphyodont dentitions. The epithelial envelope controls the position of the tooth throughout the whole process of development. Proliferations of its cells on the coronal portion give rise to buds and processes which are associated with its progressive development and change of position. These proliferations together with those from the dental lamina and surface dental epithelium form the connecting dental epithelium.

(9) Origin of successional tooth germs from proliferation of the sheath epithelium is described in some teleostomi in contradiction of Charles Tomes, who states that each successional germ is derived by a new proliferation of the surface epithelium.

(10) Attention is drawn to the very striking resemblance of the sheath epithelium of a hair follicle to that of a tooth and the manner in which each is connected with the surface epithelium. There is also a developmental similarity.

(11) Contrary to the statement of Bolk that an "enamel septum" is not found in the enamel organs of reptilia, the presence of both an "enamel septum" and an "enamel navel" are shown in *Caiman crocodilus*.

but where enamel is present on the crown, as in mammals, the sheath epithelium can be clearly defined as that part beyond the region of enamel formation.

Two groups occur according to the nature of the attachment of the tooth. On ankylosed teeth the sheath is widely open and bell shaped (figs. 5, 9, 11), but on rooted teeth it is conical in form, being narrowed at the apex (fig. 20).

At first the extension is intact forming a continuous layer of cells, later this condition may persist when fixation of the tooth is by a bone of attachment, as in acrodonts, but in socketed teeth, which are attached to the bone by a periodontal membrane as in crocodilia and most mammals, the continuity is interrupted by the formation of the principal fibres of the membrane rendering it fenestrated (figs. 20 and 21).

The group selachia appears to be an exception. The epithelial envelope in these animals (dog-fish) surrounds the developing tooth as far as the expanded base of the tooth beyond which development occurs without the influence of the dental epithelium (fig. 4).

The sheath epithelium is universally present around the implanted part of calcified teeth.

In the teleostomi development of successional germs occurs from the sheath epithelium in all the specimens of this subclass of fishes that we have examined (figs. 1, 2, 3). Charles Tomes (1876) in his classical paper on "The Development of the Teeth of Fishes" makes the statement that "in teleostei the new enamel germs are formed directly from the oral epithelium, and are new formations arising quite independently of any portion of the tooth germs of the teeth which have preceded them". This may be true only of the first tooth of a series but all successional germs are formed by a proliferation of some part of the sheath epithelium of a preceding tooth.

The opinion expressed by Tomes has probably been responsible for the generally accepted view as to the origin of the successional teeth of these fishes, that each one arises independently of its predecessor by a separate proliferation from the oral epithelium.

Von Heinke (1873), however, has described the new enamel organs of pike as being derived from older ones. This observation does not appear to have been extended to other fish. There is a remarkable resemblance between this form of origin and that seen in the replacement of a hair in mammals.

In all lower forms where the teeth are ankylosed, the sheath epithelium completely surrounds the tooth and is in continuity with the surface epithelium so that the teeth are embedded in epithelium which extends as far as the bone of attachment (figs. 8 and 9).

The sheath epithelium as it is found on the completed mammalian tooth can only be effectively demonstrated in reconstruction models which show it as an epithelial network surrounding the root. In individual sections it is seen as the familiar epithelial "rests" (figs. 20 and 21).

(4) The Connecting Dental Epithelium

This is the name we have given to the dental epithelium which connects the germs and developing teeth of a dental unit to each other and to the surface. It is formed by proliferation of the cells of the dental lamina, with some from the epithelial envelope and the surface dental epithelium. As connecting dental epithelium it consists of threads, columns or bands of cells often forming a network in mammals (the intermediary plexus of Malassez in man) (fig. 22). In polyphodonts with persistent laminæ the connexions are established and maintained by the lamina to which the developing teeth are attached until they reach the surface epithelium (figs. 4 and 5). In holostei and teleostei the connexions are brought about by the sheath epithelium of the functional tooth where proliferation of its cells may form either an epithelial bud close to it, or a column of cells leading to the new germ. This column is of varying length in different or even in the same species (figs. 1, 2, 3).

In amphibia and some reptilia (snakes) a persistent lamina provides the connexions (figs. 5, 9, and 23). In crocodile, there is constantly found a process of epithelium connecting successional germs shown in reconstructed models and photographs (fig. 23).

In diphyodont mammals direct connexion is not so easily established. The early stages are simple but the rapid proliferation of the lamina cells and the development of the connexions between the epithelial envelope of the deciduous germ and the lamina, together with the changes in the latter render interpretation difficult. Here the connecting dental epithelium is seen as a network consisting of columns or nodes if cut across. Tortuous columns do not appear to be continuous if a single section only is examined, but the examination of a series puts the matter beyond doubt. The greatest activity is in the region of the epithelial envelope (figs. 14, 15, 16, 17 and 18).

It would seem that the attachment between the connecting dental epithelium and the surface epithelium during the earlier periods is not more than a fine strand, for there

PLATE I.

FIG. 1.

FIG. 26.

FIG. 1.—Pike (*Esox lucius*).   × 30.   A, surface epithelium connecting dental units.   It forms part of the epithelial framework of a dental zone ; B, origin from the surface epithelium or sheath epithelium ; C, origin from the sheath epithelium ; D, direct origin from the surface epithelium.
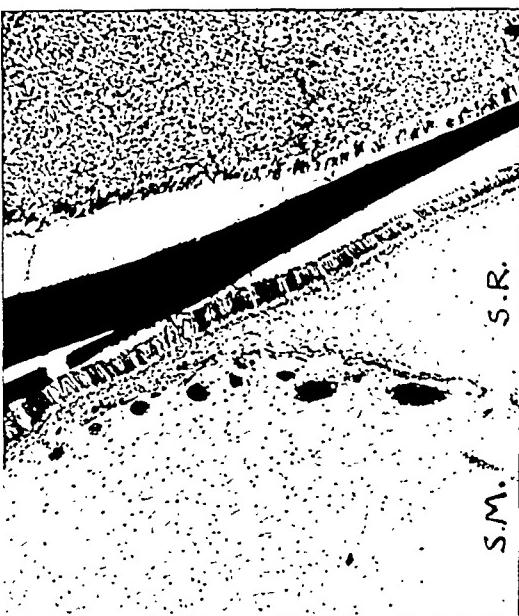
FIG. 26.—Lion (fœtal).   × 70.   Resemblance of the stellate mesoderm (S.M.) to the stellate reticulum (S.R.) Vessels intermitting with buds of the epithelial envelope in the stellate mesoderm.

FIG. 2.

FIG. 3.

FIG. 2.—Cat fish.   × 90.   A, functional tooth ; B, proliferation of the sheath epithelium from which C, a new dental germ, is arising.
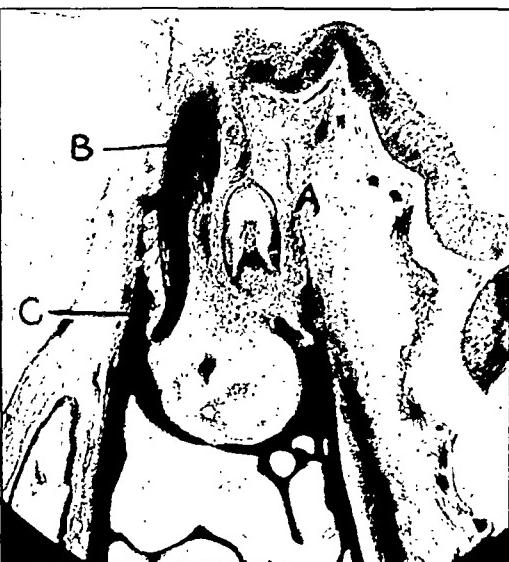
FIG. 3.—Mackerel (*Scomber scombrus*).   × 55.   A, dental germ arising from the sheath epithelium connected with B, the remnant of a functional tooth which is attached to C, the bone.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

(12) In teleostomi the sheath epithelium has an added significance as it is by proliferation of its cells and not those of the surface epithelium that the successional germs are derived. Also attention is drawn to the role of the dental epithelium in the restoration of the surface epithelium following the loss of teeth notably from the sheath epithelium, as in the eel (*Anguilla vulgaris*).

(13) The connecting dental epithelium of the mammalian dentition is complex, its proliferations play a prominent part in maintaining connexion between the developing tooth and the surface. The extent of the proliferations over both deciduous and permanent germs does not appear to be realized; but after a study of many series of different animals we are convinced that the marked proliferations are of great importance in directing the path of eruption and guiding the tooth to its correct position.

(14) The activity of the cells of the surface dental epithelium as shown by the marked proliferation over and around the erupting tooth is obviously of great importance in establishing the tooth in its functional position. We have found it in all animals but it is especially pronounced in some teleostei such as *Esox lucius, Anguilla vulgaris*, salmon, &c.

This short exposition and summary is an attempt to establish the supreme importance of the dental epithelium in initiating and controlling tooth development and eruption and the final positioning of the teeth.

LIST OF ANIMALS EXAMINED

Serial sections were cut of all that were sufficiently well fixed.

Selachii

Dog-fish—*Scyllium canicula. Scyllium catulus.*
Shark—(unknown).
Electric Ray—*Narcobutus torpedo.*

Teleostomi

Long-nosed garpike—*Lepidosteus osseus.*
Pike—*Esox lucius.*
Eel—*Anguilla vulgaris. Conger vulgaris.*
Whiting—*Gadus merlangus.*
Cod—*Gadus morrhua.*
Hake—*Merluccius vulgaris.*
Trout—*Salmo fario.*
Sea-trout—*Salmo trutta.*
Salmon—*Salmo salar.*
Chub—*Leuciscus cephalus.*
Perch—*Perca fluviatilis.*
Mackerel—*Scomber scombrus.*
Blenni—*Blennius gattorugine.*
Catfish—Species unknown.
Swallow-tailed wrasse—*Julis pavo.*
Goldfinny wrasse—*Ctenolabrus rupestris.*
Larger Bull-head—*Cottus bubalis.*
West Indian fish—Cichlid? (This fish was caught in the presence of one of us off Trinidad where the fresh water from the Orinoco extends far out to sea and is muddy. On this account in spite of being caught in the sea it was thought to be a Cichlid but was not classified.)

Amphibia

Newt—*Triton tœniatus.*
Axolotl—*Amblystoma tigrinum.*
Frog—*Rana temporaria. Rana tigrina, Rana catesbiana.*

Reptilia

Spectacled caiman—*Caiman crocodilus.*
Broad-nosed caiman—*Caiman latrinostris.*
Nile crocodile—*Crocodilus niloticus.*
Blind worm—*Anguis fragilis.*
Chameleon—*Chamœleon vulgaris.*
Wall lizard—*Lacerta muralis.*
Reticulate python—*Python reticulatus.*
Adder—*Pelias berus.*

Mammalia

Red kangaroo—*Macropus rufus.*
Bennett's tree-kangaroo—*Dendrolagus bennetti.*
Wallaby—*Macropus ruficollis bennetti.*
Pig—*Sus scrofa.*
Indian mouse deer—*Tragulus meminna.*
Rat—*Mus decumanus.*
Mouse—*Mus musculus.*
Squirrel—*Sciurus vulgaris.*
Rabbit—*Lepus cuniculus.*
Lion—*Felis leo.*
Tiger—*Felis tigris.*
Cat—*Felis domestica.*
Syrian bear—*Ursus arctos syriacus.*
Dingo—*Canis familiaris dingo.*
Hedgehog—*Erinaceus europœus.*
Lemur—*Galago moholi.*
Homo—*Homo sapiens.*

BIBLIOGRAPHY

BOLK, L. (1912) *Anat. Anz.*, **41**, Suppl. 58-68.
—— (1921) *J. Anat., Lond.*, **55**, 138, 219.
—— (1922) *J. Anat., Lond.*, **56**, 107.
GLASSTONE, S. (1936) *J. Anat., Lond.*, **70**, 260.
—— (1938) *Proc. Roy. Soc.*, **126**, 315.
HARRISON, H. S. (1901) *Quart. J. micr. Sci.*, **44**, 161.
HERTWIG, O. (1874) *Arch. mikr. Anat.*, **11**, Suppl. 1-208.
JAMES, W. WARWICK (1909) *Proc. R. Soc. Med.*, **2**, Sect. Odont., 163.
MUMMERY, J. HOWARD (1924) The Microscopic and General Anatomy of the Teeth, London.
RÖSE, CARL (1891) *Arch. mikr. Anat.*, **38**, 447.
—— (1892) Über die Zahnentwicklung des Reptilien, Berlin.
TOMES, C. S. (1876) *Philos. Trans.*, **165**, 257.
—— (1923) A Manual of Dental Anatomy, Human and Comparative. 8th Ed. by H. W. Marett Tims and C. B. Henry, London.
von BRUNN, A. (1887) *Arch. mikr. Anat.*, **29**, 367.
—— (1891) *Arch. mikr. Anat.*, **38**, 142. *Dtsch. Mtschr. Zahnheilk.*, **10**, 127.
von HEINKE, F. (1873) *Z. wiss. Zool.*, **22**, 495.
WELLINGS, A. W. (1938) Practical Microscopy of the Teeth and Associated Parts, London.
WOERDEMAN, MARTIN W. (1919) *Arch. mikr. Anat.*, **92**, 104.

PLATE III.

FIG. 6.—Human fœtus (length not known) cut vertically across two central incisors.   × 22.   Origin of a dental germ from a non-persistent dental lamina.   S.D.E., surface dental epithelium ;   D.L., dental lamina which is proliferating, passing from the thickened surface epithelium ;   C.D.E., connecting dental epithelium as a short column from the D.L. to the epithelial envelope (E.E.).

FIG. 7.—Lizard (*Lacerta muralis*.   × 55.   Sockets of discarded teeth and successional germs showing part of the epithelial framework.

W. WARWICK JAMES and A. W. WELLINGS :
   The Dental Epithelium and its Significance in Tooth Development.

PLATE II.

FIG. 4.—Dogfish. × 17. Origin of germs from a persistent dental lamina which is marked at its terminal margin by an arrow. The section is cut almost on one plane of a dental unit.

FIG. 5.—Frog (Rana catesbiana). × 250. A, persistent dental lamina with a developing tooth attached and a new dental germ forming at its terminal margin. The epithelial envelope, B, is seen in section.
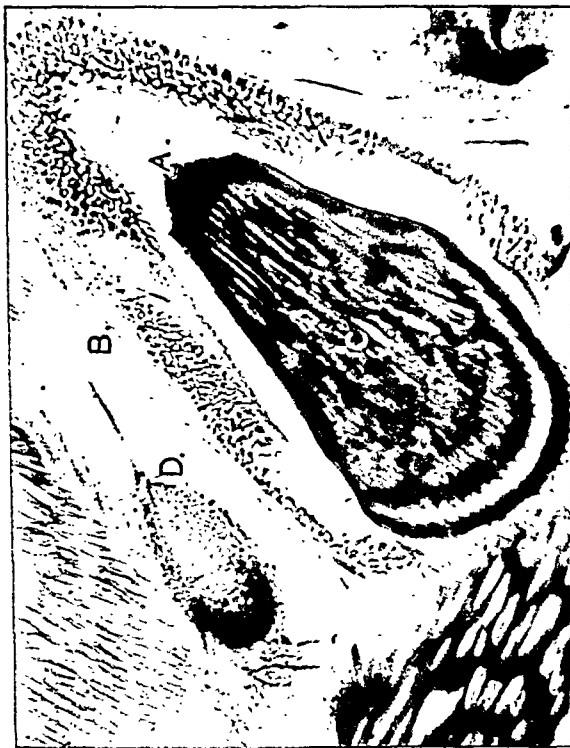
W. WARWICK JAMES and A. W. WELLINGS:
The Dental Epithelium and its Significance in Tooth Development.

PLATE V.

FIG. 11.—West Indian fish (? Cichlid). × 35. A, advanced stage of a developing tooth partly encapsuled by B, the epithelial envelope; C, formed dentine; D, young germs with connecting dental epithelium projecting from its epithelial envelope.

FIG. 10.—Caiman. × 50. Dental unit. A, functional tooth being absorbed; B, successional tooth; C, new germ with part of connecting dental epithelium at summit; D, Subgingival epithelium; E, epithelial envelope of successional tooth; F, alveolar bone; G, nerve; H, surface epithelium. The epithelial envelope of the successional tooth is uniting with the subgingival epithelium of its predecessor.

W. WARWICK JAMES and A. W. WELLINGS:
The Dental Epithelium and its Significance in Tooth Development.
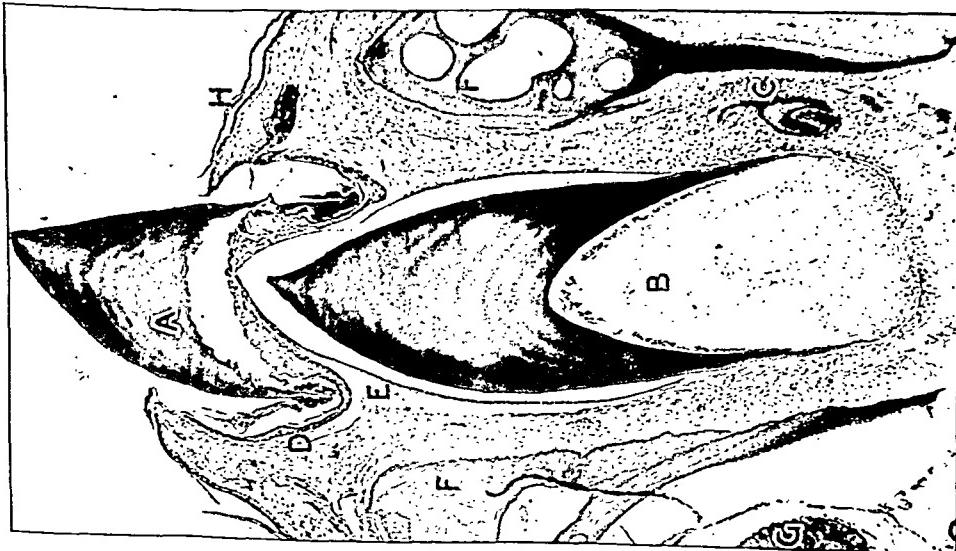
PLATE IV.

FIG. 8.—Wrasse (*Ctenolabrus rupestris*). × 16. A, functional tooth ; B, epithelial envelope, from which the tooth is lost, attached to the sheath epithelium by connecting dental epithelium ; C and D, younger germs ; E, in area of tooth development.

FIG. 9.—Newt. × 90. Showing a dental unit. A, base of functional tooth ; B, developing successional tooth attached to a persistent dental lamina, with C, the youngest member at the terminal margin.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

PLATE V.

FIG. 11.—West Indian fish (? Cichlid). × 35. A, advanced stage of a developing tooth partly encapsuled by B, the epithelial envelope; C, formed dentine; D, young germs with connecting dental epithelium projecting from its epithelial envelope.

FIG. 10.—Caiman. × 50. Dental unit. A, functional tooth being absorbed; B, successional tooth; C, new germ with part of connecting dental epithelium at summit; D, Subgingival epithelium; E, epithelial envelope of successional tooth; F, alveolar bone; G, nerve; H, surface epithelium. The epithelial envelope of the successional tooth is uniting with the subgingival epithelium of its predecessor.

PLATE VI.

FIG. 12.

FIG. 13.
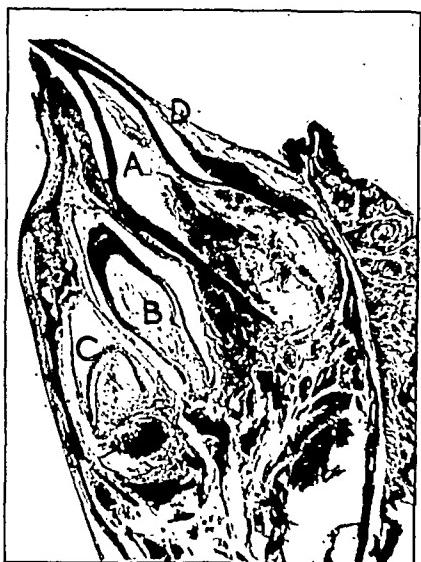
FIG. 12.—Lemur (*Galago moholi*). × 20. Showing epithelial envelopes (A, first incisor ; B, second incisor ; C, third incisor or canine) of the procumbent mandibular teeth in different stages of development ; D, epithelial envelope of first incisor.
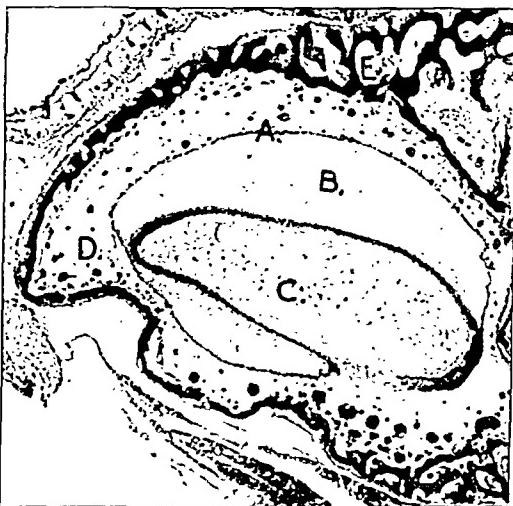
FIG. 13.—Wallaby (*Macropus ruficollis bennetti*). × 30. Transverse section of the germ of an incisor showing the epithelial envelope, A, almost enclosing it ; B, stellate reticulum ; C, pulp ; D, mesodermal tissue with many capillaries, outside the envelope ; E, alveolar bone.

FIG. 14.—Human fœtus. Vertical bucco-lingual section of mandible. × 14. A, surface epithelium ; B, proliferating dental lamina ; C, buds and processes from epithelial envelope of developing tooth with formed enamel and dentine ; D, bone of crypt.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

PLATE VII.
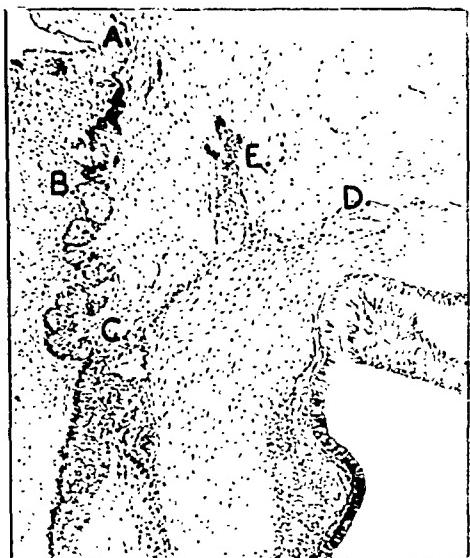
FIG. 15.   FIG. 18.

FIG. 15.—Human fœtus.   × 55.   Incisor early germ.   A, surface dental epithelium ;   B, dental lamina proliferating and forming connecting dental epithelium which is attached at C to the epithelial envelope;   D, E, proliferation from the epithelial envelope forming a projecting process.

FIG. 18.—Human fœtus.   × 335.   A, process from the epithelial envelope.

FIG. 19.—Caiman (*Caiman crocodilus*).   × 80.   A young animal.   The epithelial envelope encapsulating a developing tooth, outside the stellate reticulum.   The summit of the enamel organ shows an " enamel navel " from which an " enamel septum " passes to the inner layer of cells as is seen in mammals.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

PLATE VIII.
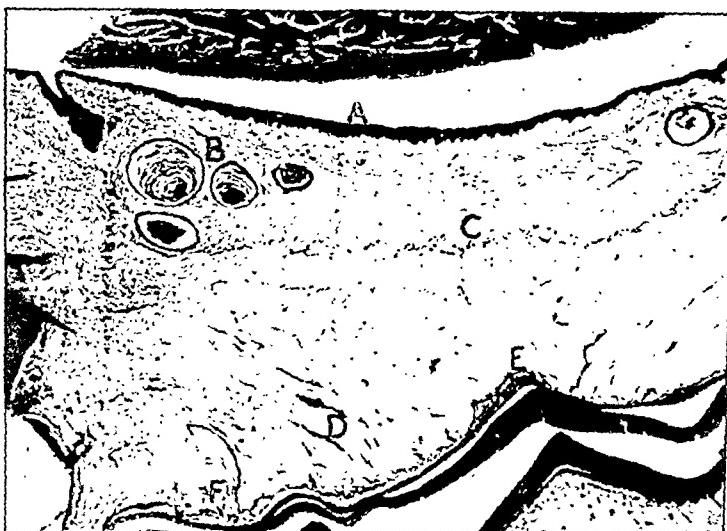
FIG. 16.—Human fœtus. × 14. A, surface epithelium; B, epithelial coils and surface dental epithelium with characteristic depression; C, proliferating dental lamina; D, buds and processes from E, the epithelial envelope; F, capillaries associated with buds and processes.
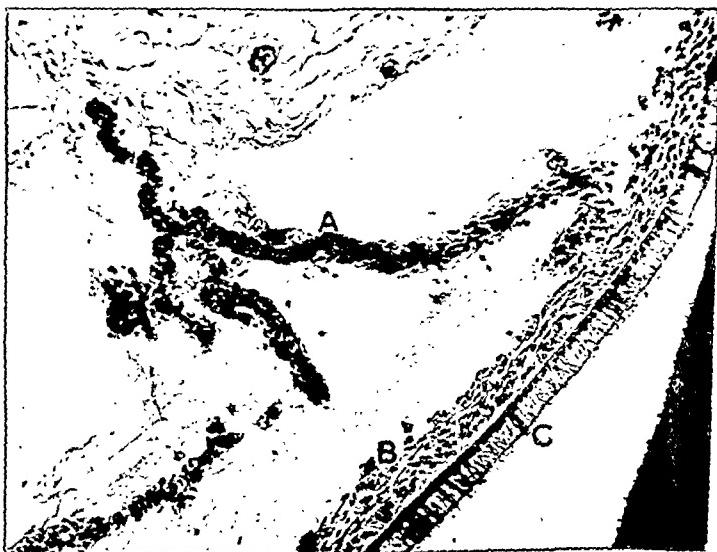
FIG. 17.—Human fœtus. × 125. Higher magnification of fig. 16, showing A, process from B, epithelial envelope; C, ameloblasts.

W. WARWICK JAMES and A. W. WELLINGS:
The Dental Epithelium and its Significance in Tooth Development.

PLATE IX.
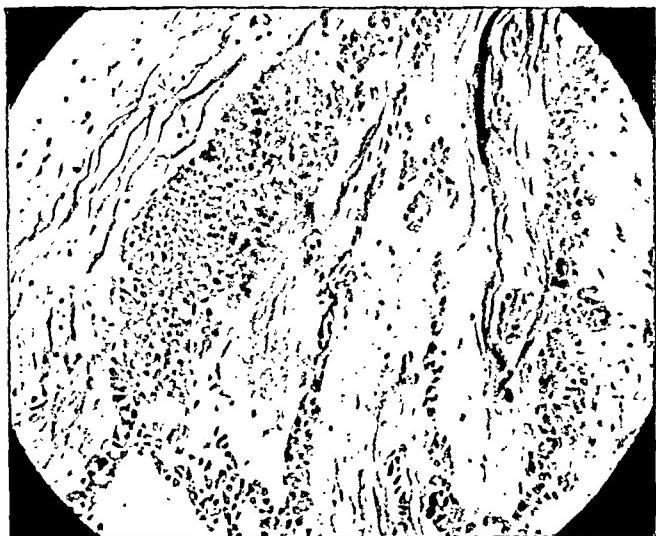
FIG. 22.

FIG. 20.

FIG. 23.

FIG. 20.—Pig. Newly born. × 11·5. Continuity between the root sheath epithelium C, which is fenestrated, and B, the subgingival epithelium with the epithelial attachment. A, functional tooth and its epithelial envelope which has almost attained its final relationship.

FIG. 22.—Human. × 225. Connecting dental epithelium which has been formed by proliferation of cells of the dental lamina.

FIG. 23.—Caiman. × 80. The connecting dental epithelium, C, passes between the epithelial envelope of the developing tooth, A, and the germ, B, with which the dental lamina, D, is just seen to be connected.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

PLATE X.

FIG. 21.—Tiger (at birth). × 30. Section of a developing tooth prior to eruption showing 1, proliferation of the surface dental epithelium above it ; 2, coronal part of the epithelial envelope which is continuous with the subcoronal part 3, the root sheath epithelium which shows fenestration. The apical mesoderm is undergoing active proliferation.

W. WARWICK JAMES and A. W. WELLINGS:
The Dental Epithelium and its Significance in Tooth Development.

PLATE XI.

FIG. 24

FIGS. 24 and 25.—Human. × 30. From the same series a few sections apart. The network of connecting dental epithelium in fig. 24 and the absence of any cells in the tissues above the tooth in fig. 25 are striking : a possible explanation of the statement that these cells disappear.

W. WARWICK JAMES and A. W. WELLINGS :
The Dental Epithelium and its Significance in Tooth Development.

PLATE XII.

FIG. 25

FIGS. 24 and 25.—Human. × 30. From the same series a few sections apart. The network of connecting dental epithelium in fig. 24 and the absence of any cells in the tissues above the tooth in fig. 25 are striking: a possible explanation of the statement that these cells disappear.

W. WARWICK JAMES and A. W. WELLINGS:
The Dental Epithelium and its Significance in Tooth Development.

[*May* 24, 1943]

Severe Retrusion of the Mandible Treated by Buccal Inlay and Dental Prosthesis

By B. W. Fickling, F.R.C.S.

(*From the Maxillo-Facial Unit, Hill End Hospital, E.M.S.*)

THE restoration of facial contour and mastication in cases of severe mandibular retrusion by means of a prosthetic appliance inserted into a buccal inlay is a well-recognized surgical and dental procedure. The dental treatment may be divided into three stages. First, a stable appliance is required to maintain in one position for six to ten days a mould constructed during the operation. Secondly, an appliance which is readily removed by the patient for cleansing, but which has sufficient fixation to withstand the tendency for extrusion during the contractile phase of healing which persists for three to four months. In both these stages the deformity must be over-corrected. Thirdly, the definitive appliance, functional, comfortable, light and yet large enough fully to restore the facial contour.

In each of the following cases osteomyelitis of the mandible in childhood resulted in collapse and failure of growth of the mandible with consequent facial deformity.

FIG. 1.—Lateral view of Case I, before, during and at the completion of treatment.

CASE I.—L. N. Between the ages of 3 and 7 this patient was under treatment for osteomyelitis of the mandible, during which time there were numerous operations, extensive sequestra were removed, and the left mandibular teeth were lost. He cannot remember being able to open his mouth.

When aged 20 he developed an alveolar abscess on the right side of the mandible. On examination, there was severe retrusion of the mandible with full cheeks, pouting lips and redundant soft tissue in the mental region (fig. 1). There was an extremely close bite and the opening of the mandible was limited to 1/16 inch on the right side and ¼ inch on the left. Under endotracheal anæsthesia the mouth could not be opened further, so the teeth involved were removed from the buccal aspect. Radiographs showed gross deformity of the mandible, both rami being almost absent (fig. 2).

On 16.9.42 Mr. Rainsford Mowlem and Mr. John Barron excised the right condyle and a spur of bone which represented the left condyle, using the post-auricular approach, with division and re-suture of the external auditory meati. Extensive fibrosis was discovered and divided. After this the mouth could be opened ½ in. and Zelex impressions were secured during the operation, for the preparation of splints.

Right

Left

FIG. 2.—Radiographs of Mandible in Case I, showing lack of downward and forward growth and absence of the condyle on the left side.

On 23.10.42 Mr. Rainsford Mowlem performed an extensive buccal inlay, a large gutta-percha mould being inserted and secured to a splint cemented to four mandibular teeth. Eight days later an acrylic mould was substituted, containing hollow spheres to make it lighter, and made as a duplicate of the gutta-percha by means of impressions obtained during the operation for insertion of the graft. After twelve weeks a new appliance was inserted constructed in two parts which, when screwed together, obtained a grip of the splint. After twenty-seven weeks the remaining erupted mandibular teeth were extracted together with the four unerupted third molars. After thirty weeks a new and more æsthetic appliance was inserted, providing much greater tongue room as a result of the loss of the four natural anterior teeth. There is now an opening of approximately 1 in. whether measured from the mandibular alveolus or the artificial mandibular incisors.

CASE II.—G. W. developed osteomyelitis of the mandible at the age of 7. Many teeth fell out and a massive sequestrum gradually extruded into the mouth and was removed. This represented the greater part of the mandible and was used at the examinations at the Royal College of Surgeons, which the patient also attended.

When aged thirty-eight the patient attended the Royal Dental Hospital complaining of indigestion and inability to masticate. There was extreme inferior retrusion with consequent fat and prominent cheeks (fig. 3). The mandible was edentulous and the posterior maxillary teeth occluded on the gum. A radiograph revealed a rudimentary mandible (fig. 4).

FIG. 3.—Anteroposterior views of Case II, before, during and at the completion of treatment.

FIG. 4.—Lateral radiograph of Case II, showing the rudimentary mandible and artificial teeth maintaining the profile far anterior to the bone. The acrylic prosthesis is radiolucent.

On 31.10.41 Mr. Rainsford Mowlem performed a buccal inlay, the mould being retained by means of a chin clamp. Stability is difficult to attain in the presence of such an edentulous rudimentary mandible. In this case a fistula developed at the bottom of the new sulcus as a result of pressure. After five weeks a denture was inserted, constructed in cascowyte on account of the closeness of the bite, the mould being of acrylic. A Kelly's paste impression was used. After eleven weeks the fistula was closed and eight months later a further plastic operation was performed to obliterate the depression in the neck caused by the attachment of the tissues to the rudimentary mandible. This considerably improved the contour. Later a permanent appliance in acrylic was inserted. She is now able to masticate all foods and the improvement in appearance is striking. In these cases successful treatment results in a marked psychological change, which is reflected in the change in facial *expression* as opposed to *contour*.

CASE III.—F. C. had measles in childhood followed by osteomyelitis of the mandible. Numerous sequestra were removed by external incision. When aged 22 there was marked asymmetry of the face, the mandible being retruded and deviated to the right, with marked flattening on the left side.

On 7.9.42 the scars were excised and the soft tissues freed from the bone. On 25.9.42 a buccal inlay was inserted from the right premolars to the left second molar, the mould being attached to a splint on the left mandibular teeth. Four weeks later a duplicate acrylic mould was inserted. Epithelialization was slow and there was suppuration at the bottom of the sulcus.

Six months later the splint was discarded and a new prosthesis inserted in the sulcus without fixation of any kind. This is extremely comfortable and causes no inconvenience to the patient.

I wish to record my thanks to Mr. Rainsford Mowlem and to all the members of the Unit, whose co-operation has made possible the treatment and recording of these cases.

Section of Psychiatry

President—W. Norwood East, M.D., F.R.C.P.

[*October* 12, 1943]

The State, The Criminal and the Psychiatrist

PRESIDENT'S ADDRESS

By W. Norwood East, M.D., F.R.C.P.

Special Consultant to the Royal Navy
Formerly H.M. Commissioner of Prisons, &c.

The task of one whose work lies within the confines of a narrow speciality and who attempts to interest those with wider activities than his own is not free from difficulty, and this is increased if his knowledge and understanding sometimes result from private statements made by men and women in explanation of conduct which has incurred legal punishment including the penalty of death. For here, as elsewhere, the physician must remember the relevant passage in the Hippocratic Oath and steadfastly refuse to "noise abroad" the things which should be kept as "sacred secrets". Moreover, a special responsibility devolves upon those who are concerned with medico-sociological problems to-day. The war of 1914-18 was followed by a marked impetus to the scientific approach to criminal problems, and the reconstruction of our daily life in the coming years will demand from those concerned with criminals, as from other specialists, well-conceived guidance which must be so clear and forceful that the co-operation of the public and administrators, as well as of the legal and medical professions, is enlisted and sustained progress established.

A prison psychiatrist, therefore, firm in the belief that physical and mental health are closely correlated with the welfare and security of society, can desire from his own profession no higher recognition of the importance of his chosen sphere of work than to be called upon to deliver this address.

THE STATE AND THE CRIMINAL

The observations of ethnologists go to show that the members of a primitive community are required to conform to ritual and observe certain rules of conduct. Similarly, cultured society requires its members to react to certain situations in accordance with approved and complicated patterns of behaviour, and the pressure of public opinion is usually sufficient to enforce the adoption of the accepted standards. If this fails the imposition of penalties may result, in the civil court if compensation to a private individual is the purpose, in the criminal court if the injury done affects the wider interests of society. The difference between crimes and civil injuries does not lie in the nature of the wrongful acts themselves, but in the subsequent legal consequences, and many criminals could be sued in civil proceedings for pecuniary compensation for the harm which they have done.

The law creates crimes since progress introduces unavoidable prohibitions, but an act may be a grave offence at one period and a trivial matter at another. Moreover, conduct may be criminal in one country and praiseworthy elsewhere. For example Hoebel points out that the killing of infants, invalids and old people, as well as the act of suicide, are forms of acceptable homicide in Eskimo society and are, in whole or in part, responses to the basic principle that only those may survive who are able, or potentially able, to contribute to the subsistence economy of the community.

Crime is often due to motives which are both qualitatively and quantitatively similar to non-criminal motives, and it is generally just as biologically normal as ordinary behaviour. Indeed, law-breaking is so common that to determine who is guiltless might be as perplexing as the unanswered question of Pontius Pilate.

Modern advances, and the recent interest in the behaviour of children and young persons who commit legal offences have caused some observers to shrink from using the word crime for the minor infractions of the law committed by juniors, and to replace it by the term delinquency, reserving the more virile term crime for major offences committed by adolescents or adults. But this is not always so, the word delinquency is sometimes used by writers for all types of offences, however serious their nature, and the word delinquent for adult criminals as well as for children and juveniles.

A crime may be regarded as an act or omission forbidden by law under pain of

punishment, and the term will be used in what follows for major and minor offences, and the word criminal will be applied to all offenders who are punishable in adult criminal courts for I believe that to euphemize here is to obscure the importance of minor social defects.

The classification of mental disorders accepted by the Council of the Royal Medico-Psychological Association in 1938, like most classifications, does not include the term "crime" or "delinquency". The Report on Mental Health by the British Medical Association Committee, issued in 1941, however, includes "delinquency" in the list of mental disorders. The Report states that the conditions enumerated overlap one another and that there are differences of opinion as to what the diagnostic terms cover. To catalogue delinquency without qualification as a mental disorder with oligophrenia, the psychoneuroses, schizophrenia, affective psychoses and the rest invites hostile criticism from informed observers, and well-considered opposition from lawyers and administrators whose daily experience discredits crude over-statements and fallacious generalizations.

To suggest that delinquency is necessarily a manifestation of mental disorder not only leads away from truth but serves to impede, rather than assist, the scientific approach to the problems involved.

Lombroso declared that crime was a natural phenomenon and that it was as necessary as birth, death or conception. However this may be, standards of approved behaviour vary from time to time, and the innermost thoughts and undisclosed activities of our friends and acquaintances may evince unexpected deviations without transgressing the ordinary accepted standards of the average man.

Crime may be the response to a high sense of duty towards an individual or to a group, and it sometimes happens that an offender believes his act is right and proper although it is wrong in the sense that it is punishable in law. This result is unfortunate for the offender as well as for society since the acceptance by the law-breaker of the fact that his offence is wrong and his punishment just is, as the late Lord Haldane pointed out, an identification of his will with the will of his fellowmen, and a step towards compensating persons he has injured.

Although there is no justification for the belief that crime, *per se*, is an indication of mental disorder, there can be no doubt that repeated criminal behaviour by the same offender may be the result of mental abnormality. If normal human conduct is developed through the stages of pleasure-pain, gain-loss, public approval-disapproval to the higher level in which right prevails because the intention to adopt exalted standards and ideals is carried out regardless of the effect upon pleasure-pain, gain-loss, approval-disapproval, we may believe with Harold S. Hulbert that the development of the habitual criminal is fixed at the gain-loss level, and that his crimes are related to the fixation.

The legal conception of guilt is now independent of the idea of morality, and we cannot base our efforts at reformation on training for citizenship divorced from moral standards. It is, therefore important to remember that modern research challenges the question as to whether compensation is the usual sequence in human affairs. Wood considers the correlation between mental and moral qualities is contrary to the popular idea. Thorndike states:

"... in human nature good traits go together. To him that hath a superior intellect is given also on the average a superior character: the quick boy is also in the long run more accurate; the able boy is also more industrious. There is no principle of compensation whereby a weak intellect is offset by a strong will, a poor memory by good judgment, or a lack of ambition by an attractive personality. Every pair of such supposed compensatory qualities that has been investigated has been found to show correspondence."

Chassell finds:

"The principle of the mutual relationship of desirable qualities still remains unchallenged: as far as the relation between morality and intellect is concerned, correlation and not compensation is the rule."

The official classification of the Home Office divides crimes into six main groups which, however, are not mutually exclusive, viz. offences against the person, offences against property with violence, offences against property without violence, malicious damage to property, forgery and offences against currency, other offences. This classification lacks significance for the psychiatrist since the legal and official approaches differ from the scientific approach. The legal interest in a killing, for example, may depend mainly upon the guilt of the accused and the differentiation of murder from manslaughter. The medical interest will be chiefly concerned with the personality of the offender, both generally and also at the time the crime was committed.

For medical purposes crimes can be conveniently classified into acquisitive, aggressive, sexual, gregarious and the like, according to the instinct involved. This approach directs

immediate attention to the emotional qualities accompanying the crime and the disposition of the offender.

Official statistics do not allow any precise figure to be given concerning the number of criminals whose offences are attributable to any particular instinct. Not only is there overlapping but the differentiation is often incomplete. For example, the figures for "breaking and entering" leave doubt as to whether the criminal belongs essentially to the acquisitive, aggressive or sexual group. The figures cannot be taken at their face value, for although the great majority of offences are apparently acquisitive the study of individuals often shows that a seemingly acquisitive offence is really due to the self-preservative or parental instinct, and that some cases of murder or assault, burglary, theft, arson and the like are primarily sexual offences and only incidentally associated with the aggressive or acquisitive instinct. Again, the figures relating to crime and criminals are always open to the criticism that they never can include crimes which are not reported to the police, or the offenders who are not even suspected of committing crime.

The legal and administrative classifications of criminals need not delay us, the latter is amended from time to time in order to comply with progressive measures of administration. It was customary in the earlier years of the present century to discuss criminals under the headings of accidental, occasional and habitual, and these terms still represent, broadly, some features of criminality. In the scientific study of the criminal, however, it is important to consider the mental condition of the offender as well as the occasions which prompted the crime, and whether he is a nuisance or a menace to society before a decision can be reached regarding his capacity for future social adaptation.

From the medical point of view criminals can be classified broadly under the headings of normal, subnormal, mentally defective, psychoneurotic, psychopathic and psychotic. But the groups sometimes overlap, and no psychiatric classification is likely to give entire satisfaction until the dividing line between mental diseases and character anomalies is established with some degree of precision apart from personal estimates.

The groups enumerated above and their sub-groups are fairly well defined by psychiatric practice, and I have suggested elsewhere that a criminal psychopathic personality may be defined, tentatively, as a person who, although not insane, psychoneurotic or mentally defective, is persistently unable to adapt himself to social requirements on account of quantitative peculiarities of impulse, temperament and character which may require specialized medical and rehabilitative treatment instead of, or in addition to, the ordinary methods of punishment before his social reclamation is likely to be effected.

Criminality is sometimes roughly measured by the nature, number and variety of offences which have been previously committed. The degree of turpitude in different classes of crime, as well as of different offenders in the same crime group, cannot be accurately assessed unless the individual offender and the circumstances associated with the crime are closely studied. Criminality and turpitude are not measured necessarily by the prescribed legal punishment. Murder, for example, must be punished with greater severity than theft, but the murderer who is not insane and who has been reprieved is unlikely to repeat his offence when he regains his liberty, whereas the criminal tendencies of the thief not infrequently prompt him to steal again as soon as an opportunity to do so presents itself.

The positive school of criminology considered crime was forced upon those who became criminal because of their inherited traits, but it is unnecessary to regard this view at any length, or call attention to recent studies in heredity when addressing an audience of psychiatrists, for our daily estimations of behaviour show that it is sometimes mainly endogenous, and at other times chiefly exogenous. Moreover, the interactions between heredity and environment are recognized by all observers to-day. Character and conduct may effect changes in the environment; conversely, environment influences character and conduct. It will suffice here to note the well-known facts that crimogenic traits which in themselves are socially useful may produce anti-social effects when synthesized in the offspring; that although many important new facts are emerging from recent investigations concerning the interactions of the activities of the endocrine glands the resulting knowledge is, so far, of little practical value in the treatment of criminals; that crime in the individual is attributable to numerous causes and that no single cause is ever present; that the persistent criminal is on the whole more concerned with self in isolation than with self in the social setting, and often shapes his behaviour on phantasy, rationalization and projection; that personality takes time to reach its full development; and that practical experience seems to show that in a majority of cases as one gets older personality is a more important crimogenic factor than environment.

It is often stated with truth that criminal conduct is a maladjustment at the psycho-

socio-biological level, but it is not always true to say that it is the result of the incapacity of the criminal to make an adequate social adjustment. The majority of persons found guilty of substantial offences for the first time, who were followed up, were clear of further charges during the subsequent five years, and proved themselves capable of social adjustment. The study of crime and criminals has suffered from the overstatements of doctrinaires. The intricate subjects requiring exploration demand a clear recognition of the fact that the connexion of crime with mental abnormality is only a part of the problem. The association of crime and mental normality is also important and widespread. It is equally deserving of further research.

THE STATE AND THE PSYCHIATRIST

This rough blackboard outline must serve to indicate some of the aspects of crime and criminals with which the psychiatrist is immediately concerned. Before going further it is advisable to consider briefly the relations of the State to the scientist, and since my working life has been happily spent in official duties my judgment may be biased in favour of the executive and administrative authorities. I therefore turn to the views of four eminent men of science.

Wilfred Trotter declared in 1933:

"The senior professions of the Church and Law have always had prestige enough to enable each of them to keep a finger firmly and consistently in the governmental pie. They have, therefore, been able to see to it that any duty that was laid upon them should be set off by a corresponding privilege or immunity. The lowly and junior profession of Medicine, unlike its proud and elder sisters, has had no direct part and no direct influence in the work of government. It has, therefore, had to submit to its duties being piled up as occasion arose, with no resource for securing a due compensation of privilege and immunity except such slender sense of natural justice as governments possess, and their occasional doubts about the prudence of overloading a willing beast. These resources have shown all the ineffectiveness we might have expected. The result is that at a time when it is no longer possible to conceal the wholly unique importance of medicine for the very existence of social life, that profession finds itself of all professions the least in command of social prestige, the least privileged, the most exposed and the hardest worked. I do not mention this state of affairs because I think it is to be deplored. I do not think it is to be deplored. The evolutionary cause that has put the profession of medicine where it is may not be the one that would have been pursued by conscious wisdom, but it has had the result of putting medicine in the very small class of professions that, in this tame world, can still be called jobs for men".

Julian Huxley stated in 1934 that he had become

"more than ever impressed with the fact that both our existing structure of civilization and our hope of progress are based on science, and that the lack of appreciation and understanding of science among business men, financiers, educational authorities, politicians and administrators was a serious feature in our present situation".

Sir A. Daniel Hall in 1937 said that

"the working men of science are called upon to organize in order to make their point of view prevail in the affairs of the State. I recognize how alien this is to the temperament of leaders of the world of science. They ask only to be allowed to remain in their laboratories, there to secrete knowledge without bothering about its purpose. That they conceive is their function in the community, but in the end such detachment means slavery and the destruction of the freedom of thought upon which science itself depends".

And he recalls the disparaging remark of an American politician, a candidate for the Vice-Presidency, at the time President Wilson was running for President, "Brains", he said, "I can buy any of that lot for twenty dollars."

A. G. Tansley speaking at Oxford University, in 1942, declared that:

"the current education of the men who are entrusted with the forming of Government policies has almost ignored and frequently despised science".

Ministers of State generally lack scientific education or achievement, but the knowledge and experience of the expert can never relieve the Government of the responsibility for judgment and decision in the direction of affairs. The executive is, indeed, sometimes willing to accept the advances in scientific knowledge which can be put to practical use. Whilst, however, a scientific training creates a habit of forming decisions upon reason it is not itself entirely free from emotional influence. Moreover, the scientist usually limits his explorations to a narrow speciality and this is becoming increasingly prevalent. Even when his results are positive, and can be applied to practical purposes, they may be unavoidably subordinated to wider interests or financial restrictions, and the situation of the moment must be focused clearly. This done there remains, and always will remain until a remedy is found, dissatisfaction on the part of the scientist who is affronted at the reluctance so often shown to utilize scientific knowledge to the full because it lacks popular appeal.

It was left to Ivan Petrovitch Pavlov to say in 1935 at Ryazan, his birthplace in Soviet Russia:

"... Formerly science was divorced from life and alienated from the people, but now I see it is otherwise—I see the whole nation respects and appreciates science. I raise my glass and drink to the only government in the world which could bring this about, which values science so highly and supports it so fervently—to the government of my country".

It is becoming increasingly important for the scientist in a democratic State to make contact with the general public as well as with the governing authorities, since the latter may be unable to advance too far ahead of public opinion. Statesmen are few, politicians are numerous and are interested in the popular vote, and the scientist may find his valuable contribution neglected unless the public are interested in his work and force the politicians into activity. The difficulty lies less in the acquisition of knowledge than in obtaining quick and effective public action. It will be remembered that Sir Edward Mellanby discussed the question at some length in a recent Harveian Oration.

Although as doctors we may be less effective than legislators in the prevention of crime and the treatment of criminals, it is right to recognize the fact that we are concerned with individuals rather than with groups, and that the offenders who come under our special care are usually the most difficult and the least responsive. They are sometimes referred to us only in the last resort, and we must serve them with optimism free from exaggeration, inspired by hope and encouraged by goodwill.

Physicians must avoid any suspicion of self-advertisement, but a legitimate occasion to make contact with the public arises when evidence is given in a court of law concerning the mental condition of an accused person. Lawyers, administrators and mastermen of psychiatry are sometimes shocked by the unwarranted explanation of criminal conduct given by journeymen psychiatrists. It is important to check the natural tendency to overinterpret criminal behaviour in terms of mental abnormalities which are found in non-criminal cases. Opinions should be withheld until all the available facts concerning the circumstances of the crime are known and correlated with the findings of the medical examination. The offender must be appraised as a whole, and not according to the dictates of a medical fashion which may be, for the moment, interested in an isolated part of mental activity. I venture this trite remark because incorrect diagnoses are sometimes made regarding the mental condition of accused persons as a result of placing undue reliance upon hearsay, upon incomplete documentary evidence, and upon academic theories.

There can be no doubt that opinions are occasionally peddled in public with real detriment to criminology and psychiatry. But it is the duty of journeymen psychiatrists as well as the mastermen to enhance the reliability of medical evidence, and we must not assume greater knowledge than we possess regarding the diagnosis, prognosis and treatment of the pathological criminal. Moreover, we must not promise dividends we cannot pay. The law and the executive may wish for a clear-cut medical solution for dealing with an abnormal criminal, but our knowledge is the result of studying types of offenders with similar abnormalities, and we must often err if we are too insistent in the belief that the individual offender before us will necessarily conform to the usual pattern of his type.

Evidence in a criminal court may, for some reason entirely outside the medical purview, obtain widespread publicity, and may have real propagandist value which is all the more effective if it is clearly and simply stated. It is a misfortune that the difficulties inherent in the changing views regarding psychological functioning sometimes prevent even the mastermen from using ordinary terms of expression. It is an added misfortune that many mastermen of psychiatry are so actively engaged that they seldom have time to spare to stand back from their work, like the painter at his easel, and consider whether it is good.

We cannot disregard the fact that some psychologists who have no medical qualifications and no training in psychiatry are too ready to make a diagnosis concerning the mental condition of persons they examine. I am not here concerned with the relation of the medical profession to the non-medical psychologist, but I have for over forty years had exceptional opportunities to study at close hand the evidence given in the criminal courts concerning the mental conditions of accused persons, and it would be simply untrue to say that it was always satisfactory. I refer to this matter because the number of non-medical psychologists seems likely to increase, and their divergent views are likely to confuse juries if they are expounded in the criminal courts. I believe that courts and juries will be best served in this matter by refusing to accept the opinions of non-medical psychologists and psychotherapists.

I go further. If progress in this direction is to be achieved in the post-war period I

believe that evidence concerning the mental condition of accused persons, and the manner of their psychological functioning should be accepted only from experts who are registered medical practitioners and that medical men who have no special qualifications as psychiatrists, however eminent they may be in other branches of medicine, should steadfastly refuse to be drawn into expressing opinions in the witness-box concerning the difficult matters which may arise in regard to the association of mental disease and crime.

It is sometimes proposed that a psychiatric and psychological examination should be carried out on all persons who come before a criminal court. In my view the scientific approach to criminal problems and the study of the criminal is hindered by extravagant statements of this kind. Is it conceivable that all the offenders referred to previously, who were found guilty of substantial offences and were clear of any further criminal behaviour during the subsequent five years, required a special psychiatric investigation? Can we believe that the large number of motorists who come before courts of summary jurisdiction should, or would, submit themselves for examination, or that there are ever likely to be a sufficient number of psychiatrists to carry out the proposal? Progress is best served by recognizing the hard realities which confront us, and by eschewing the fanciful and subversive assertions of doctrinaires.

The protection of society from the criminal and of the criminal from society concern both the State and the psychiatrist. The latter is sometimes not free from bias in favour of the criminal, and this seems to be almost inevitable since the training of the physician generally leads him to put the interest of his patient before other considerations. But in a criminal case the wider interests of society cannot be impoverished in favour of the offender, and any attempt to do so will eventually injure him as well as the society in which he lives.

On the other hand, too much stress cannot be laid upon the importance of maintaining the independence of the psychiatrist whose researches and opinions should not become subservient to the political fashion of the moment, as appears to be the case in Nazi-Germany. At the same time the psychiatrist must bear in mind the fact that public opinion in England still lags behind the progressive penal policy of the executive authorities.

It is sometimes suggested that the mental condition of an accused person should be taken out of the hands of the jury, and that a medical referee sitting with the presiding judge should determine the issue. I believe this suggestion is thoroughly mischievous. If the results of a psychiatric examination are to be informed and purposive the accused must feel that the medical examiner is able to extend to him a bond of human sympathy and understanding, a realization of his difficulties and temptations, and a willingness to explore the winding paths as well as the direct road which led up to the crime. If the medical referee is merely to assess the value of the documentary evidence and the opinions of the expert witnesses he will often find himself uncertain, dissatisfied and sometimes wrong unless he makes a personal examination of the offender. But it is quite impossible to carry out a psychiatric examination satisfactorily in court. I have in mind particularly the art of the psychiatrist, for in criminal cases the art of examination and the facility with which the examiner obtains rapport with the accused are often more important than abstruse scientific learning. We should not expect a modern Grinling Gibbons to carve a masterpiece of delicate and elaborate detail in wood unless he applied the artist's touch as well as the workman's hand directly to his material. Neither should we believe that the psychiatric referee would be able to work upon the delicate materials which make up mind and personality unless he applied his art, as well as his science, under the most favourable conditions available, and in immediate contact with the accused. On the other hand, if the medical referee had to examine the accused outside the precincts of the court the practice would present disadvantages and be inferior to our present methods.

There would seem to be less medical objection to a procedure which restricted the duty of the jury to finding the prisoner guilty or not guilty of the crime, leaving the question of insanity and irresponsibility to a medical tribunal before the court determines the sentence. The Secretary of State is already directed to set up such a tribunal in certain circumstances after the sentence has been delivered in capital cases (Section 2 (4) of the Criminal Lunatics Act, 1884). This clearly presupposes entire confidence in the psychiatric opinions at the disposal of the State.

It should be remembered that there seems to be nowhere any willingness to transfer the functions of the court and jury to the psychiatrists, and I do not believe that psychiatrists wish this duty to be imposed upon them. I believe we recognize that our training and experience are not necessarily the best to apply to wider issues, and that as psychiatrists we may be able to carry a case only partially forward to the final con-

clusion. Different interpretations of the significance of the same set of facts may be made by warring expert witnesses, and an intolerable burden would be placed upon psychiatry in its adolescence if it had the last word in a criminal court.

For example, many authorities consider sadism may be expressed by normal or abnormal behaviour. It may be the only discernibly unusual feature associated with a crime, and the immediate challenge may concern merely a question of degree. Against this must be balanced all the other relevant factors which go to show that the accused is fully responsible. Are these factors to be outweighed by the divergent opinion of one of the disputing psychiatrists if he favours the accused, and considers that the degree of sadism manifested in the crime indicates a pathological condition which should excuse the criminal from the consequences of his act?

Again, other sexual perversions may also be the result of a constitutional anomaly, but is the psychiatrist the person to decide whether its overt expression should be more tolerated than that of sexual offences which are not due to perversion, and may be more urgent than the less forceful drives of many perverts? If so, what standards should he apply? Further, competitive jealousy is a common cause of murder. Is this to be regarded by itself as an indication of abnormal mental functioning in the circumstances, and so excessive that the accused ought to be considered irresponsible? If so, is the experience of a psychiatrist on this particular issue more reliable than the combined experience of twelve jurymen and an experienced judge who, unlike most psychiatrists, is constantly studying at first hand and in considerable detail the emotions and reactions of large numbers of criminals?

Let us at once recognize the fact that criminal responsibility is a legal concept which the public understands and of which it approves, and that so far psychiatry has not replaced it by anything more precise or practical. Let us remember that the law is applied with elasticity in suitable cases. Let us regard criminal responsibility and the culpability recognized by medical men as two different things, and by leaving the former to the lawyers have more time to study closely the medical conception of culpability, for this is likely to become increasingly important with the crystallization of our knowledge regarding minor mental abnormalities. Perhaps as we approach nearer to the heart of the matter we may be more able to assist the lawyers in reshaping the doctrine of criminal responsibility as set out in the McNaghten Rules.

Meanwhile, it seems logical and just to detain the sociopathic offender, who is not insane or mentally defective but whose culpability is lessened on account of a minor mental disability, in a special type of establishment which is not an ordinary prison or mental hospital but a custodial institution in which judicial restrictions and modern therapeutic measures are combined.

THE CRIMINAL AND THE PSYCHIATRIST

At the beginning of the present century psychiatric interest in the criminal was much occupied with the association of mental defectiveness and crime. The next period was largely concerned with separating the mentally defective offenders from the ordinary criminal population, and was particularly useful in placing the position in correct perspective. At one time it seemed that some enthusiasts wanted us to believe that prisons were almost unnecessary and that most of them could be profitably converted into institutions for defectives. It can be confidently stated that if the prison medical officers had allowed themselves to be corrupted by these views the study of minor mental and character abnormalities associated with crime would have been deferred. We seem now, generally, to have reached a period when informed reason has displaced uninformed credulity, and have learnt that the problem of crime and mental defectiveness, although important, is comparatively small.

In the Annual Report of the Prison Commissioners for 1932 I recorded three instances where the prisoners for some time had been regarded as mentally defective. As a result of prolonged observation during which a longitudinal view replaced a transverse section of their histories, and a change over from anti-social to social behaviour occurred, one prisoner was found to have suffered from mental conflicts during childhood which affected conduct until they were resolved. The repeated offences of the second were probably due to periodic physiological imbalance which was subsequently adjusted by marriage. In the third case the slow development of the personality which gave rise to the diagnosis of mental defectiveness was eventually caught up, and the youth became a normal man. Cases like these are particularly instructive for they dispel complacent diagnoses and emphasize the importance of prolonged clinical study.

The rearrangement of modern psychiatric thought regarding the genesis, association, and classification of mental abnormalities has favourably influenced forensic psychiatry. Different views may be held regarding these matters and the psychiatrist must have

no illusions. The interpretation of newly found knowledge is often more difficult than the ascertainment of new facts. Abstruse psychological hypotheses, although useful on suitable occasions, often have little practical bearing on the crime under consideration.

The psychological treatment of crime is so recent that its scope is still uncertain. It is not to be recommended lightly or without discrimination, and we may expect for some time to come that unsuitable cases will be suggested for treatment as well as those which are suitable. The study of minor mental disorders, as well as the introduction of new methods of treatment in later years have opened up new possibilities in the scientific attack on crime. A psychological investigation, however, may explain conduct but does not necessarily excuse it; and the comfortable doctrine of self-expression, regardless of the interests of society, causes distrust and opposition if it discounts the value of self-control and public security. There is a growing tendency in the criminal courts to consider the criminal more than the crime, but the welfare of the criminal must often be subordinated to the wider interests of society. Imprisonment may be necessary for public reasons in spite of the fact that non-custodial measures have been recommended by the psychiatrist. Conversely, detention over a prolonged period, with or without special psychiatric rehabilitative treatment, may be desirable from the medical aspect, but may not be justified by the nature and circumstances of the crime.

Perhaps the most outstanding feature of the association of the modern psychiatrist and the criminal is the recognition of the importance of the emotional rather than the intellectual genesis of crime. It had, of course, long been recognized that certain crimes, particularly those of violence and sex, were primarily emotional; but it is comparatively new for offences such as theft, burglary, forgery, false pretences, arson and the like to be linked up with unapparent emotional activities.

The study of sexual crime, in particular, has contributed much in recent years to a better understanding of instinctive action when directed towards criminal purposes. It is not too much to hope that future study relating to the other instinctive activities will assist in the better understanding of criminal behaviour. We may assert with some degree of confidence that the usual penal methods will often prove to be inadequate to prevent the commission of sexually perverted crime. We may hope that research directed towards the study of perverted activity associated with the acquisitive, aggressive, parental and gregarious instincts will enable us to determine whether the usual penal methods will fail here also. Further knowledge may clear the way for the introduction of new methods for treating non-sexual perversions and for protecting society against them.

Psychiatrists reduce the probability of criminal behaviour by effecting the social adjustments of their patients at Child Guidance and Psychiatric Clinics. The difficulty of assessing results, however, is increased by the fact that although anti-social tendencies may seem to be removed the patient sometimes remains more potentially criminal than his fellows when contact with him is lost.

This does not, of course, in the least diminish the importance of the psychiatric approach to crime, or the value of the psychiatrist in the diagnosis, prognosis and treatment of abnormal mental states connected with crime, or indeed the need for psychiatric advice in regard to the disposal of the pathological criminal. But it does emphasize the importance of research regarding normal as well as abnormal criminality, and the need to avoid dogmatic opinions and unwarranted complacency. Justice can be done to the abnormal offender only if the psychiatrist is consulted with reference to his personality, for the criminals who do not respond to the usual penal methods are not only the most recidivistic but also the most menacing to society, the most difficult to understand, and the most in need of help. I urge this view because I believe that the whole problem of the mental treatment of crime is likely to be jeopardized if the public come to think that the psychiatrist always wishes medical treatment to replace the ordinary measures of criminal justice. At the same time, as psychiatrists, we must deplore the general backwardness in the early recognition and treatment of mental illness as well as of criminal tendencies.

My own investigations in later years have impressed me with the importance of co-operation with research workers who are not primarily interested in crime or criminals, but whose special knowledge can be advantageously associated with that of the prison psychiatrist. I have in mind, for example, joint research into the crime rates in the two sexes, the incidence of different crimes in different age-groups, the psycho-socio-economic causes of prostitution, the investigation of perversions other than sex, the exploration of minor personality deviations, the significance of volition on criminal behaviour, a long distance view of the results of the psychological treatment of crime,

the biochemical associations of criminal behaviour and the like. I believe that such co-operation, if wisely exploited, will in future take us much further than it is possible for prison research workers to reach alone, and will add still further to our knowledge and understanding of the criminal.

However this may be, we should remember Ryle's admonition:

" The scientific ideal in medicine does not of necessity demand intensive abstract study of minutiæ, prolonged specialized inquiry, or training or discovery by experiment alone. Rather does it require insistence on truth, correction of error, an understanding of the methods whereby truth is ascertained, an ability to sift evidence, and an appreciation of ' wholes ' and of those co-ordinating activities which determine the nature of things, and without some understanding of which our study of ' parts ' may become an enfeebling or confusing rather than an enlightening process ".

The State, the Criminal and the Psychiatrist

The ultimate dispute concerning free will and determinism need not concern us here, as in the practical affairs of life the disputants act upon the assumption that they are able to select their course of action. Neither need an exhaustive survey of the principles involved in the term "punishment" detain us. The protection of society and the prevention of crime, as well as the treatment of the criminal, are recognized to-day to be more closely interwoven than has been sometimes assumed.

The State acts, and must act, upon the assumption that men and women are mentally normal, until the contrary is proved. The psychiatrist may have difficulty in accepting the conception of normality for one of its inseparable characteristics is occasional odd behaviour, and no man is himself always. Nevertheless, our immediate concern is the amount of deviation from a hypothetical standard pattern of thought and behaviour in a hypothetical standard man which can be allowed in the clash between personal and community interests.

The State, representing Corporate Society, is clearly entitled to adopt rules which are considered necessary for its own protection and are accepted by the majority. It must therefore have the right and power to enforce its principles upon anyone who accepts the advantages of living within this protection but transgresses the standards of conduct required. At the same time educational, economic, and other improvements in later years have brought with them a more humane approach to the problem of crime, and science has contributed to a better understanding of the criminal.

The State, the Criminal and the Psychiatrist may be associated together before, during or after the trial. Reference has been made already to the preventive effect of early treatment. On arrest the accused may be remanded on bail or in custody in order that he may be medically examined. During the trial an elaborate system known as the law of evidence, as well as special criteria regarding criminal responsibility which culminate in the verdict, govern the procedure. After the trial the association may be concerned with the appropriate treatment of the offender in a mental hospital, out-patient psychiatric clinic or penal institution. The different procedures relating thereto need not be considered, but some of the proposals put forward in the Criminal Justice Bill, 1938, which were being considered by Parliament at the outbreak of war are of particular interest to the psychiatrist.

One of the main objects of the Bill was to provide for the abolition of imprisonment as a method of treatment for young offenders convicted of such offences as are dealt with by courts of summary jurisdiction, and to substitute alternative methods. It proposed to authorize the provision of special institutions to be called " Remand Centres " to which young offenders remanded or committed for trial in custody should be sent instead of to prison. It also proposed to give improved facilities to courts of summary jurisdiction to obtain a medical report on the mental condition of an offender without remanding him to prison for the purpose, the court being empowered to remand the offender on bail with a requirement that he submit himself to medical examination at approved institutions or by approved persons. At the same time it was proposed that all expenses and fees incurred should be met from public funds. Another clause in the Bill proposed that courts of summary jurisdiction should be enabled to make an order for the treatment of an offender who is certifiable as insane in the same way as they can at present make an order for the treatment of an offender who is mentally defective. Further, it was proposed that probation orders might include a provision requiring offenders who were not insane or mentally defective, but who required and were susceptible to treatment, to submit themselves to mental treatment. It also provided for the payment of such treatment by the probation committee.

In accordance with the recommendations of the Departmental Committee on Persistent Offenders, upon which I had the privilege to serve, the Criminal Justice Bill proposed in lieu of, and not in addition to, sentences of imprisonment or penal servitude, two new types of sentence:

(a) Sentences of corrective training for a period of not less than two and not more than four years on persons between 21 and 30 years of age, whose records, character and habits are such as to make such sentence expedient for the training of the offender; and

(b) Sentences of corrective detention for a term of not less than two and not more than four years on persons over the age of 30, if by reason of the offender's criminal antecedents and mode of life such a sentence is expedient for the protection of the public. For certain types of offenders with records of repeated crime it is proposed that such sentences may exceed four but shall not exceed ten years.

Enough has been said to ensure the goodwill of psychiatrists in furthering the intentions of the Bill to grapple still more closely, individually, efficiently and humanely with the ever-present dilemma of penal reform.

As a result of the investigation into the psychological treatment of crime at Wormwood Scrubs prison, Hubert and I recommended the establishment of a special institution, under the administration of the Prison Commissioners, for abnormal and unusual types of convicted offenders. I have also referred to this in a later publication. This institution would serve as a clinic or hospital where convicted prisoners could be investigated and treated by psychotherapy and other means, and as a centre for criminological research as well as for co-ordinating the various aspects of after-care organization. In the institution selected cases could live under special conditions of training and treatment. Many who are unsuitable for, and unmodified by, the re-educative and rehabilitative influences of the modern prison system would be allocated to this section. Its aims would be to amend behaviour by the application of psychiatric experience. The institution would also serve as a colony in which a further type of offender could live who had proved unable to adapt himself to ordinary social conditions, but for whom reformative measures, however specialized, seemed useless and the inflexibility and restrictions of ordinary prison life inappropriate. A branch institution would serve as an observation and treatment centre for those who, because of minor mental abnormality, appeared to be unsuitable for, or had failed to respond to, ordinary Borstal training and for various reasons were considered unfit for early release on licence.

CONCLUSION

The scientific approach to crime and the scientific treatment of mentally abnormal criminals are urgently important and eminently practical matters, and will demand further attention in the post-war scheme of social justice. I have attempted in this address to indicate briefly the trend of modern thought, as I see it, concerning some of the intricate problems involved. In my judgment some of these problems lie within the wide borderland between mental disease and anomalies of character, rather than in the territory dividing mental health from mental illness.

However this may be, our part must be carried out in the spirit of scientists who are able to take long views and perceive the shape of things to come, who are concerned with men and women and the naked facts of life and living as well as with the inexorable realities of disease and death, who are willing to serve both State and law-breaker with all the energy and goodwill of our humanistic tradition, and who, in spite of disappointments and rebuffs, maintain an abiding faith in man's usefulness to man. Moreover, as trustees of progress and truth we must not let our legatees remind us of the Writing on the Wall, for " The Moving Finger writes; and, having writ, Moves on. . . ."

REFERENCES

BRITISH MEDICAL ASSOCIATION (1941) Report of Committee on Mental Health.
CHASSELL, C. F. (1935) The Relation between Morality and Intellect, New York.
EAST, W. NORWOOD (1943) Chadwick Lecture : " The Differentiation, Prevention and Treatment of Anti-Social Behaviour Disorders," *Brit. J. Inebr.*, 40, II, 35.
—— and HUBERT, W. H. de B. (1939) The Psychological Treatment of Crime, London.
——, STOCKS, P., and YOUNG, H. T. P. (1942) The Adolescent Criminal, London.
HALDANE, Lord (1925) Internat. Penitent. Cong., London.
HALL, Sir A. DANIEL (1941) Knowledge and Power (What Science Stands For), London.
HOEBEL, E. A. (1941) *J. crim. Law & Criminol.*, 31, 6.
HULBERT, H. S. (1935) Crime Conference, Michigan.
HUXLEY, JULIAN (1934) Scientific Research and Social Needs, London.
KENNY, C. S. (1909) Outlines of Criminal Law, 4th ed., Cambridge.
LOMBROSO, C. (1911) Crime, its Causes and Remedies, translated by H. P. Horton, London.
MELLANBY, Sir E. (1939) Harveian Oration : " The State and Medical Research," Edinburgh.
PAVLOV, I. P. (1941) Conditioned Reflexes and Psychiatry, translated by W. H. Gantt, London, z.
PRISON COMMISSIONERS (1932) *Annual Report*.
RYLE, J. A. (1936) The Natural History of Disease, London.
TANSLEY, A. G. (1942) Herbert Spencer Lecture : " The Values of Science to Humanity " London
THORNDIKE, E. L. (1920) *Harper Hosp. Bull.*, III, 227.
TROTTER, W. (1941) Collected Papers, London.
WOODS, J. A. (1919) *J. Hered.*, 10, 84.

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

[*October* 15, 1943]

The Cancer Problem from the Point of View of the Young Gynæcologist

PRESIDENT'S ADDRESS

By MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

CANCER is a research subject, the treatment of which must be carried out by a team, and the team should decide from time to time how a certain type of cancer shall be treated. In order to take his or her place in the team the young gynæcologist must not only be a good gynæcologist and an expert surgeon, but must have a considerable knowledge of radiotherapy, and be able to take an intelligent interest in the advances that are taking place in the histology, pathology and ætiology of this disease. It is also of very great value if the gynæcologist has a working knowledge of radiophysics, but in any case he must work in close collaboration with a physicist. The treatment of cancer—both private and hospital patients—should be carried out in a fully staffed, and properly equipped, institution.

Nature of cancer.—At one time it was thought that the nature of a malignant cell could be demonstrated by the abnormalities which might be seen under a high power lens of a microscope, and, although it is undoubtedly true that certain abnormalities are frequently present in the anatomy of a malignant cell, yet no one abnormality is always present, and, indeed, any of the histological abnormalities seen in a malignant cell may be found under certain conditions in non-malignant cells. It is now realized that the malignant process lies in the physiology of the cell, and this idea is endorsed by the late Professor Ewing who states that the physiology of a tumour cell is more important than its structure. There is an increasing amount of evidence that in some cells the abnormality of the physiology can be rectified, and the malignant cell be stimulated to attempt some measure of differentiation. This, I think, is a new point of view to some of us and is one that the young gynæcologist should keep in mind.

Ætiology

Volumes have been written on the ætiology of malignant disease, much of which makes fascinating reading; for instance, the works of Bittner, who reduced the susceptibility of a 100% cancer strain in mice to 50% by feeding the young on the milk of a low cancer strain of mice. It is impossible, however, for a practising gynæcologist to do much work on ætiology; which is a whole-time job, but its study shows us *the danger* of jumping to conclusions. For instance, it is statistically true that there are a greater percentage of multiparæ suffering from carcinoma of the cervix than nulliparæ, but it is very questionable whether this fact has anything to do with trauma. Again it is statistically true that carcinoma of the body of the uterus occurs more frequently in nulliparæ but no explanation is yet known.

Resistance

The idea that the body may have a resistance to cancer is not new, but it is questionable whether sufficient thought is given to this side of the problem. Most

of us have seen how the peritoneum readily forms adhesions in order to cut off malignant disease. In one case I did a laparotomy for carcinoma of the body of the uterus, and found secondaries spread out over the whole parietal peritoneum. Some of these were excised and microscopically they proved to be degenerated malignant cells.

The fact that the peritoneum can destroy papillomata which have spread from a papilliferous ovarian cyst suggests that the "resistance" must be looked for not so much as a specific action against cancer cells, but as the power of the tissues to control any abnormal growth. This power to control further growth is seen in the healing of a wound. The factors starting the process of healing are well known, but little is known of the factors which stop the process when once the healing is complete.

Again, every gynæcologist has seen a small carcinoma of the vulva, with large masses in the lymph glands and no evidence of growth between the two sites. It is difficult to believe that the lymphatic channels are such perfect tubes that every cell gets carried along and arrives in the lymphatic gland without being arrested on the way. The work of Gray showed that malignant cells wander in and out of these channels. This suggests very strongly that the tissues outside the glands very often can deal with the cancer cells, but once inside the glands the cells grow with ease.

Another example of secondaries finding a suitable place in which to survive is shown in bone metastases. It is true that recent experiments have been published which suggest that these are carried there by the blood-stream, but the fact remains that, in some cases where there are extensive secondaries in bone, there are very few surviving deposits outside the bone.

The question of radio-sensitivity is bound up in the question of resistance to malignant disease.

Early Diagnosis

Nearly every day of the year, certainly every week of a working year, we say, "If only this patient had sought medical advice earlier we should have had a chance"; but very little is being done to remedy this state of affairs. Before the war the British Empire Cancer Campaign organized lectures to lay audiences and over twelve hundred such lectures were given. At first very considerable opposition was raised on the grounds that such lectures would turn the population into neurasthenics. I am convinced from the numerous letters that were received from people who attended these lectures that the exact opposite is true. As soon as people are able to talk freely about cancer in the same way that they talk about other diseases, then—and not until then—will it be possible to do away with the fear and ignorance which are so largely responsible for the late diagnosis of cancer even in accessible sites. It is essential that many more lectures to the public should be given after the war. But how can the individual gynæcologist help? We all have many cases of patients suffering from cancer-phobia, and some people believe that it is possible to laugh away this fear from the minds of such patients. Nothing is further from the truth. The only way we can help them is to say after a careful examination: "There is no evidence of cancer or tumour present." It is essential to use the word "cancer" in order to help the patient. If time permits the patient should be told something of the early symptoms of the more common types of cancer, care being taken to emphasize that other diseases may cause these symptoms, but that in any case they should be investigated: for instance, lumps in breast, vaginal hæmorrhage, or hæmorrhoids. Further, if they are worried at any time they should be encouraged to visit a doctor once a year and to explain that they are anxious to have an overhaul. Unfortunately when early diagnosis is obtained the good is often nullified by the fact that the patient's name is put on a waiting list, and, if the gynæcologist is not interested in cancer, the name will remain on the list for weeks before the patient is admitted. *Cancer should be regarded as an acute disease, and waiting lists as a blot on our civilization.*

Treatment

The difficulty of treating cancer arises not only in finding a treatment that will have an effect, but also in assessing the effect that the treatment has on that growth. In most diseases it is easy to treat a certain number of cases within a comparatively short time, and, if the signs and symptoms disappear, that patient is said to be cured. Such a simple procedure is not possible in the case of cancer, and some other assessment of the effect must be sought. It is generally agreed that a five years' survival rate gives a rough idea of the effect of treatment, but, in order to use this method for comparing the efficiency of different techniques, it is necessary to have at the start the same biological and other conditions present in the two series of cases. This difficulty is one of the factors that in the past has caused such heated arguments on the respective merits of surgery and radiotherapy in carcinoma of the cervix. Another difficulty arises

from the fact that in the course of five years any treatment is liable to undergo evolution, the changes produced being based not so much on scientific grounds but rather on the intuition of the surgeon. Although these difficulties cannot be entirely overcome, yet a great deal can be done by keeping accurate records. In my experience it is essential to have a stenographer in the theatre with a form containing multiple headings. The stenographer calls out the headings and the operator dictates the note. Unfortunately, this procedure is impossible during the war owing to shortage of labour.

Recently Dr. Spear and Dr. Glücksmann have suggested another criterion, which makes it possible within a few weeks of the start of treatment to assess the effect on the primary growth. This method consists in counting the entire cell population of an area of tissue taken from the growing edge of the growth before and after irradiation, and then determining the number of cells in each of four categories, viz. dividing, degenerating, resting and differentiating cells. By plotting the results as percentages against time on a graph, it has been found that the curves show certain characteristics by which the effectiveness of the radiation can be judged.

Action of Radiotherapy

This work has also thrown some light on the way in which radiotherapy brings about certain results. The cells of some malignant tumours have a tendency to go on dividing and thus produce an increase in the number of anaplastic cells, while those of other tumours differentiate. This capacity for differentiation varies for different tumours and also among different cells of the same tumour. In the opinion of Spear and Glücksmann, irradiation, while destroying some cells outright, helps other cells to differentiate. Thus, where a capacity for differentiation exists, irradiation may be used to transform the malignant mass into a relatively benign "lump".

This problem of how radiotherapy brings about certain results has been studied for many years. It was soon realized that cancer and other quickly growing tissues were more sensitive to radiotherapy than normal tissues. The question then arose as to whether the irradiation acted directly on the cells or indirectly through its effect on the surrounding tissues. It is not possible in a short general review to go into all the evidence for and against a direct versus an indirect action of radiotherapy, but the outstanding fact that large growths are usually more difficult to eradicate than smaller ones, in spite of the fact that each individual cell in the two tumours receives the same amount of radiation, suggests that there is an indirect action. Ten years ago ("Radiotherapy in the Diseases of Women," London) I summed up in favour of the indirect action being the more important factor, and suggested that successful radiotherapy was a matter of restoring the balance of power in favour of the normal tissues. I have seen no reason to change those views.

The young gynæcologist who is undertaking radiotherapy must think seriously about all these theories and must search for an optimum dose of irradiation which will encourage differentiation. It is possible that a large dose may have the opposite effect.

Value of a physicist.—In carrying out radiotherapy it is essential to be in close contact with the physicist. For instance, in every case of advanced carcinoma of the vagina or vulva in which radiotherapy is used my colleague from the physics department attends in the theatre, and we plan the treatment so as to get the required number of r of irradiation to a certain area.

Dangers of Radiotherapy

There are still a certain number of practitioners who are using radium or radon with very little knowledge of the subject. One of the great dangers is the fact that the bad results of treatment, so often due to ignorance, do not appear at once, but begin to show after many months or even years, and the mistakes in technique are therefore not so obvious to the practitioner as would be the case in bad surgery. Some people think that legislation should be introduced to prevent people who are ignorant concerning radiotherapy from using it. It is a very difficult question and probably time and education will be required to solve the problem.

Pain in advanced cases of cancer.—One of the things that makes cancer feared more than any other disease is the pain that is so often associated with the advanced stages. It is a provision of Nature that when pain ceases the victim very rapidly forgets about it, but this is a disadvantage, for it is very difficult to take sufficient interest in other people's pain. I do not suggest that medical people are callous about the pain that their patients suffer but there is a tendency to be content with ordering some morphia and to leave it at that. Pain is a physiological problem and, although good work is being done here and there by individuals on this all-important problem, yet I look in vain for a

committee or group of workers who are devoting their whole time and energy to find a method for the abolition of pain without leaving the victim an unconscious mass of useless flesh.

Cancer Act

The Cancer Act of 1939 will prove to be one of the very greatest benefits in helping to solve the cancer problem. The Act itself is short and somewhat unimpressive, but everything will depend on the way it is carried out. The Act compels certain of the local authorities to submit schemes to the Ministry of Health that will provide efficient diagnosis and treatment for cancer patients within their area. It does not require each local authority to have a separate scheme; on the contrary powers are provided to compel them, where desirable, to set up joint schemes. They are partly responsible for financing such schemes but are enabled to recover from the Treasury some of the money expended. The Act also compels local authorities to consult with the voluntary hospitals and other medical bodies within their boundary. Since most of the treatment of cancer has been, and is being, carried out in the voluntary hospitals, the Act provides a golden opportunity for the voluntary hospitals to get together and draw up schemes which will also embrace municipal hospitals and their services, and will provide a first-class cancer organization. *I believe that any large hospital which decides to adopt an isolationist policy will eventually lose all its cancer patients.* Such schemes will provide for diagnostic and consultative centres, treatment after consultation between the surgeon and radiotherapist, efficient follow-up departments, statistical departments for the whole area as well as for the individual hospitals, educational lectures to the public, and a number of other services in connexion with cancer. Such an organization will provide not only for more efficient routine treatment than is obtained at present by most patients, but an ever-increasing opportunity for planned research.

Finally, to quote the words of my late colleague, Herbert Williamson, "medicine without research is like a body without a soul".

Section of Physical Medicine

President—P. BAUWENS, M.R.C.S., L.R.C.P.

[*October* 20, 1943]

Electrodiagnostic Interpretations in Nerve Lesions [*Abstract*]

PRESIDENT'S ADDRESS

By P. BAUWENS, M.R.C.S., L.R.C.P.

THE ·potentials locally required to initiate nervous impulses or muscular contractions are minute and there is little difficulty in producing them in isolated preparations. The current densities needed in the immediate neighbourhood of the structure to be stimulated are readily obtained by the use of small currents. Considerably larger currents are required in order to obtain the same densities around this structure when it lies deeply buried and is surrounded by other tissues. Only a small fraction of the total current used is then effective. The major portion is wasted by leakage along inert structures or perversely engaged in stimulating other excitable tissues.

The main features which characterize the two types of muscle fibres involved in our problem are: quantitatively, the I/T (Intensity Duration) curve and qualitatively, the brisk as distinct from the sluggish response of the muscle fibre. When a muscle is homogeneously composed of one or the other type of fibre it is easy to ascertain to which it belongs. It is where there are mixtures of the two that difficulties of detection and interpretation present themselves. In order to extract the maximum useful information from the transcutaneous method of muscle testing, it is necessary clearly to visualize the effect of electrical stimulation on muscles compounded of varying ratios of the two types of fibre.

To this end, it is important to possess a vivid conception of the changes resulting from a progressive increase in the quantity of denervated muscle fibres with the consequent proportionate decrease in normal fibres. These modifications are expediently conceived and expressed in terms of twofold I/T curves.

Fig. 1 consists of some sets of curves graphically depicting representative phases during this gradual change. In the case of mixed fibres, two separate curves are shown. Each

d ---- DENERVATED   n ——— NORMAL   ⤳ LOGARITHMIC TIME SCALE IN SECS. ⤳
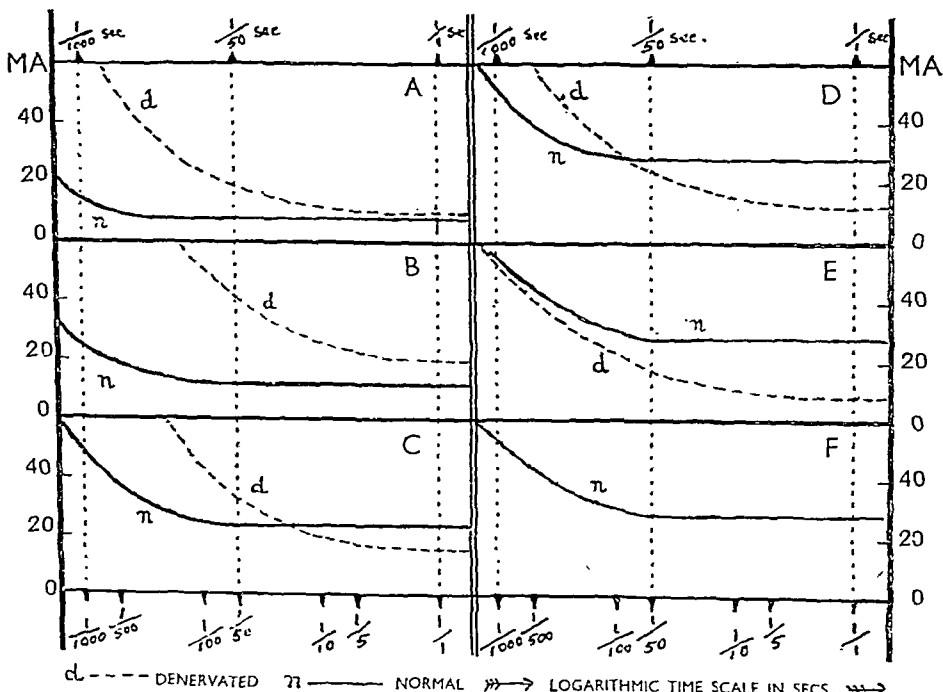
FIG. 1.

is the I/T curve of the aggregate of one type of fibre at a moment when axon degeneration is fully established and no recovery has occurred. The durations of flow of the current are measured in seconds along the abscissa on a logarithmic scale, while the threshold currents in ma.s appear along the ordinates on a linear scale. In fig. 1 (A) the typical I/T curves of a normal and of a fully denervated muscle are shown for the sake of reference. It should be noted how the d-curve rises progressively with decreasing durations while the n-curve has an initial portion which is parallel to the abscissa. In fig. 1 (B) are shown the I/T curves of the normal and denervated components of a muscle whose motor nerve has been partially destroyed. In this particular case, there is but a small proportion of denervated muscle fibre and the normal fibre component has a lower threshold for all durations than the denervated component.

It is clear that the denervated fibres will remain undetected, and that with currents below their own threshold, they will act merely as inert by-pass resistances which will entail the application of larger currents in order to stimulate the normal fibres. Even when using currents of sufficient intensity to provoke a response in the denervated fibres, their action will be masked by the dominant action of the normal fibres. Despite this, the presence of small numbers of denervated fibres may, under favourable conditions, be revealed by the expedient of applying the electrodes over both ends of the muscle, so that the current field invests the whole muscle. This longitudinal position of the electrodes favours the direct stimulation of muscle fibres as distinct from indirect stimulation through the nerve with a single electrode applied over the motor point. Only when the longitudinal reaction is sluggish can it be regarded as significant of the presence of denervated fibres.

In fig. 1 (c) the number of denervated fibres is greater and that of normal fibres proportionately smaller. As a result, the I/T curves cross, which means that with the longer durations the typical sluggish response of the denervated fibres will be in evidence whereas the brisk response which characterizes the normal fibres will be elicited with the brief impulses. Fig. 1 (D) merely shows I/T curves of a muscle with a still greater proportion of denervated fibres. It should be noted that this has led to a shift towards the shorter durations of the point at which the curves cross. This is manifested by a prevalence of sluggish reactions over a larger range of impulses of long duration. In fig. 1 (E) the I/T curve of the denervated muscle fibres has for all durations, a threshold well below that of the normal fibres. This implies that by stimulation over the muscle itself, no normal fibres can be detected although they might be revealed when the actual nerve is stimulated. Fig. 1 (F) shows the I/T curve with the features of normal fibres only, but with a high threshold value for all durations. This might occur in the presence of œdema when currents of high intensity are required, or in the same muscle as the preceding one (fig. 1 (E)) if no recovery of the denervated fibres had taken place and all these had now undergone complete fibrosis.

These various curves are of some interest when examined in conjunction with the method adopted for producing the reaction.

It is evident that if they could be reconstituted in their entirety—as shown—they would afford valuable information from a diagnostic if not from a prognostic point of view. Unfortunately, of the twofold curves—the most important ones—only the portions nearest the abscissa are obtainable by straightforward methods allowing of comparison.

In an attempt to accumulate as much data as possible from which to reconstitute these curves, I devised an apparatus [*Proc. R. Soc. Med.* (1941) 34, 715] which gives out single impulses, rectangular in wave form and the duration and intensity of which could be independently controlled. By using pentode valves in the output circuit, it was found possible to measure the current delivered and to ensure that this remained unaffected, within reasonable limits, by fluctuations of resistance.

After a number of experiments which involved the plotting of complete I/T curves of both normal and denervated muscles, it was decided for practical purposes to restrict the measurements of thresholds to three different durations.

Durations of one second, a thousandth of a second, and an intermediate one of a fiftieth of a second were decided upon. These particular values were selected because: The one-second duration gave all the information which interrupted galvanism affords and was of sufficient length for the estimation of the rheobase. The thousandth of a second was not chosen solely as a concession to the classical method. It was found from experimental work that in normal muscles the threshold for this impulse rarely exceeded double the rheobase, as can be seen from the n-curve in fig. 1 (A). This impulse of a thousandth of a second can moreover be identified with the traditional faradic impulse; with the added advantage that it can be assessed in milliamperes. The function of the intermediate duration of a fiftieth of a second is not immediately apparent. To envisage its utility it is necessary to realize that in the normal muscle the threshold for this intermediate impulse is still the same as the rheobase, but in

the denervated muscle the threshold for this intermediate impulse is more often than not at least double the rheobase. This can be seen from the curves in fig. 1 (A).

Again if the response it elicits is definitely recognized as brisk or sluggish, one is able to decide on which side of this duration the curves cross. If they cross as in fig. 1 (C), the response at a fiftieth of a second should be brisk and as might be expected it is found that the threshold for a thousandth of a second is less than double the threshold at a fiftieth of a second. The reason for this is apparent from the curves in fig. 1 (C). When the curves cross as in fig. 1 (D), the reaction to a fiftieth of a second should be sluggish and the response to a thousandth of a second should be well over twice that of the threshold at a fiftieth of a second.

No electrical examination is complete unless it consists of stimulation of the nerve trunk itself—preferably above the level of the lesion. This should be followed by faradic and galvanic stimulation of the motor points of different muscles supplied by the nerve. If the apparatus for doing so is available, the relative values of the threshold to both these stimuli should be estimated. The discriminating position of the electrodes for faradic and galvanic stimuli should be noted as well as the character of the responses elicited. The condition of the nerve should be assessed only when all data are correlated.

At times the findings are at variance with other evidence of accepted views. A good example of this type of conflict is the co-existence of lack of voluntary power and good nerve conduction, as evidenced by a powerful reaction in muscles when the appropriate nerve is stimulated above the site of the lesion. Whether this can be invariably explained on psychological lines is debatable. My own view is that more attention should be paid to the effect of injury on the part played by the afferent fibres of the nerve through which the patient is made conscious of the existence of his muscles. A partial answer to this paradox may well lie in this direction.

Risks of misinterpretation due to anomalous innervation are minimized if the possible alternative nerve is stimulated when suspicion is aroused. Cross-innervation is so prevalent in the hand that the effects of stimulating both the ulnar and the median nerve at the level of the wrist should be investigated as a matter of routine. Electrically speaking, the hindrances to transcutaneous electrical stimulation of muscles and nerves are: high resistance in series, and low resistance in parallel with the excitable tissue to be stimulated. The first of these acts as an impediment to the passage of the current and therefore demands the application of high e.m.f.s.; the second acts as a by-pass and compels one to employ large currents. In the deeper tissues the current density will to some extent be influenced by the presence of intermuscular fascial planes, blood-vessels, bones and adipose layers, thus it may be assumed that in normal circumstances some portion of the field will have a higher density than another and that this core of high density will cause the electrode position to have some slight directional, and selective effect. The motor points of muscles must be explained in terms of areas on the skin which bring this core of high density into the most advantageous position for stimulating the nerve supplying the muscle. When a nerve has degenerated the motor point loses its significance and becomes less critical.

It is probable that anomalies of distribution account for some of the differences noted in connexion with current threshold measurements in bulky and small muscles. In a large muscular mass where the electric field between the two electrodes is at liberty to expand it does not necessarily follow that using twice the total current causes doubling of the original current density at all points throughout the muscle, as would be the case with small muscles such as the interossei which are situated between two bony structures of high resistance.

Of all the factors which hamper muscle testing, œdema holds pride of place. When present, the excessive intercellular fluids act as low resistance paths in parallel with the tissues to be stimulated. The application of Ohm's Law explains why a higher current has to be used in a low resistance in order to obtain the necessary potential differences along it. A very marked increase in the blood content of muscle has a somewhat similar effect. I was able to demonstrate in a limb, which had a grossly defective blood supply due to a brachial plexus lesion, that an increase in the circulation produced by raising its temperature in a short-wave field, brought about an apparent decrease in the excitability. Apparent, because an analysis of the I/T curves revealed that the chronaxy was considerably lower in the warm limb although the threshold currents were higher (fig. 2).

It is unfortunate that when electrically exploring nerves, we have to rely upon sight and touch in order to detect the responses. To be visible or palpable, a large number of fibres have to be brought into action. The number of fibres required will depend on a number of factors of a mechanical order ranging from stiffness of various structures to tendon discontinuity.

In threshold measurements, where minimal responses have to be observed, the tension on the structures concerned and hence the position of the limb, are of some importance.

When concomitant contractions of other muscles due to spread of the stimulus occur, and provoke movement of tendons and of joints, the greatest caution has to be exercised in order to avoid being misled. Cold, too, increases stiffness and slows down contraction. It tends to cause a normal muscle to react sluggishly, at times simulating the typical
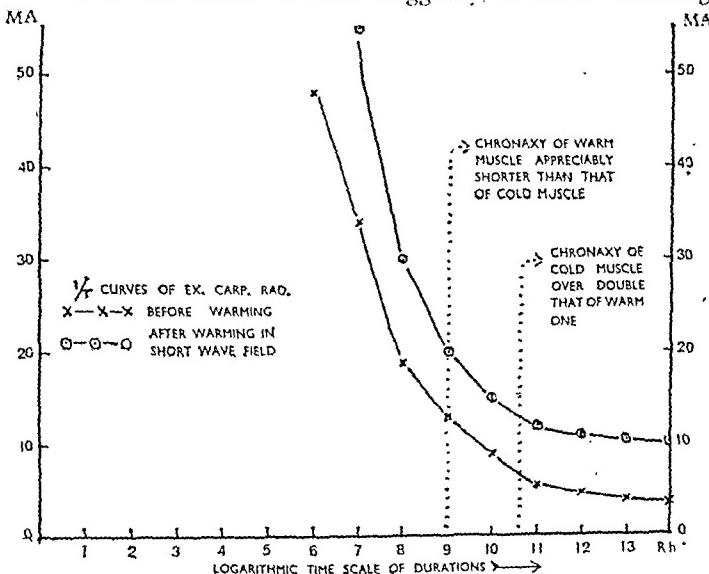
FIG. 2.

reaction of a denervated muscle. Many problems would be solved if instead of having to detect muscle contractions we could detect action potentials.

Curiously enough, sensory losses which almost invariably accompany nerve lesions can be a source of error. The presence of anæsthetic areas over the muscle to be tested enables one to use currents of much higher densities than would otherwise be tolerated by the patient. In consequence, a response to faradic stimulation is sometimes obtained in denervated muscles with a faradic current of unusually high intensity.

Some perplexing phenomena occasionally make their appearance. Of these, mention must be made of the sluggish contraction sometimes obtained as the result of faradic stimulation of the nerve or over the motor point of a muscle. My interpretation of this occurrence is that a few intact nerve fibres enable one to cause the contraction of the corresponding normal muscle fibres, whose movements act as a mechanical stimulus to the hyperexcitable denervated muscle fibres. It is significant that when this type of reaction is elicited, the muscles concerned are relatively easy to stimulate by percussion.

When stimulating a muscle with threshold faradic and galvanic currents, it is occasionally observed that entirely different bundles of muscle fibres respond to these two stimuli. This is clearly significant of partial denervation.

Before the stage of recovery is reached—that is, during the static stage—it is possible to visualize a muscle consisting wholly or partly of the only two types of muscle fibre—normal and denervated. This simple conception unfortunately becomes one of great complexity at the moment when an increasing number of muscle fibres are regaining their nerve supply. Nor is this surprising, for it is inconceivable that a muscle fibre should, at one moment, affect the characteristics of a denervated fibre and an instant later, those of a normal fibre. There must be a transitional state with fluctuating characteristics. Their I/T curves of which we know little, probably are responsible for the confusion and erratic behaviour encountered at this particular juncture.

A puzzling aspect of nerve regeneration is the frequency with which return of voluntary power precedes that of the response to faradic stimulation. Physiologists divorce the properties of conduction and excitability in nerves. It is therefore not surprising to find them returning separately. Excitability of nerves to electrical stimuli must be intimately connected with the integrity of the polarizable surface in the nerve fibre. Consequently it is not far fetched to postulate that nerve fibres and their sheaths regain the requisite electrical properties independently from axon regeneration.

Section of Ophthalmology

President—F. A. JULER, F.R.C.S.

[*October* 8, 1943]

DISCUSSION ON BURNS OF THE EYELIDS AND CONJUNCTIVA

Surgeon Rear-Admiral Cecil Wakeley, in opening the discussion, said: The problem of burns of the face and eyelids has been a very important one during this war and the last. In the last war, in the Navy, we had over 6,000 cases of burns, 95% of which affected the face and hands. In the Services, whether in the aeroplane, the tank, or the large or small ship, the face and hands suffer most severely. After the battle of Jutland we had something like 650 cases at the hospital where I was stationed, and these included a large number of burns. The first-aid dressing in those days was picric acid, but the cases in the battle of Jutland showed that this was of no use whatever, because when put on and left on it coagulated the skin to such an extent that a second degree burn was converted into a third degree burn when the dressings were removed.

In one such case of a second degree burn we treated the man with saline packs. After three days he had a certain amount of œdema of the eyelids, but otherwise the case was proceeding perfectly well, and at the end of ten days it had cleared up and there was no permanent disability.

Another patient had complete skin loss round the eyes as a result of a burn. In this case grafting was not done, and severe contractures remained.

In 1916 we realized that there were two fundamental things in the treatment of burns: (1) Elimination of sepsis; (2) Skin grafting for the third degree or deep burn.

After the battle of Jutland we devised an anti-flash gear for the face made of aertex material impregnated with an anti-heating substance to be worn by seamen.

Soon after the beginning of this war there was an undue number of facial burns which were the result of the men having the face completely unprotected. We had such a spate of cases that at the end of 1939 we devised an extra protection for men who did not wear a gas-mask. It consists of cellulose acetate goggles and aertex heat-resisting material for the nose and mouth. It can be stowed away in the man's steel helmet. Since we have introduced this protective device our incidence of burns of the face has been very small indeed. But in the Mediterranean Fleet it has seemed to me that the only thing which can induce the men to use the protection provided is to have had some first-hand experience of the danger. By far the greatest proportion of the cases are produced by exploding bombs. The bomb may not have touched the patient at all, but the effect of the blast is to split the skin, and to produce a superficial burn of the hair and face. There are usually other lesions as well. Patients treated with triple dye jelly have done extremely well.

In a bomb-flash burn the blast may also cause the skin to split. Some of these little lesions of the skin go down a quarter of an inch, but the face is so vascular that practically no scarring is experienced from the effect of such burns, and there is no permanent disability. They are usually treated with triple dye jelly. The œdema which is seen at first soon clears up.

An interesting case was that of a Russian rating in a certain submarine who started to clean the switchboard with brush and water. This of course short-circuited and he got an electrical burn of his face. Some of these burns went through the whole thickness of the skin. He was treated only with sulphathiazole cream, but we were able to get him to hospital within half an hour of the accident. There was the usual œdema of the eyelids, which cleared up and the ultimate result is extremely good, with no scarring.

In the treatment of burns, there is a vast difference between the case which is brought to hospital within half an hour or an hour of the accident and the case which does not reach hospital for five or six days. In the Royal Navy to-day 50% of our casualties due to burns occur in smaller ships which have no medical officers on board and often cannot

reach port for five or six days. In 1939-40 half the burns cases on these small ships died. By the time the men reached hospital they were moribund; we then gave up the use of tannic acid and started to use such a coagulant as the triple dye or gentian violet, and we found that our mortality was reduced to 5%. But with the increase of our corvettes we have used in these small ships the sulphonamide preparations. The trouble always is that a layman cannot distinguish between a deep and a superficial burn, and therefore we have some cases which were wrongly treated and which died simply of sulphonamide poisoning. For that reason we persist in the small ships in using a coagulant which prevents excessive fluid loss and is also antiseptic.

At the beginning of the war we thought that every case of burns should have intravenous plasma, or saline, and two out of three cases of burns admitted to Haslar at that time were treated in this way. To-day we are giving only one in ten intravenous therapy, and that is due to the fact that we have impressed upon the medical officers and the nursing staff the instruction that burn cases should be given fluid by mouth. When there are 50 or 60 such cases to deal with—the highest number we have ever had in one day was 90—some definite and quick treatment is necessary, as a hæmoglobin estimation of all these cases four times a day is obviously impossible. Common sense and clinical acumen are far more important in saving life than scientific investigation; the main thing is to save as many lives as possible. Moreover, if a series of patients in a ward for such cases find that they are to have intravenous therapy they think they are going to die, whereas if they are asked only to drink a sweetened fluid the picture is very different.

Shock.—In the Navy we take the view that morphia will never kill a man who is in pain. As to the application of heat in shock I have heard it stated that the clinician is rather apt to overheat his patients who are suffering from shock. That may be so in some cases, but I myself have never seen a patient who was very badly shocked suffer from too much heat. As soon as the patient's clinical condition has been got back to something like normal the heat should by all means be reduced, but if a man who has been in the water and has been badly burned with oil fuel is received in a shocked state, the greater and the more immediate the heat treatment we give him the better. An attempt to warm him up very gradually will never succeed.

With regard to coagulants, it has been said that a patient can die from the amount of fluid which he loses from the burned area or from the fluid which shifts from the bloodvessels into the tissue spaces. If one has got means of treating shock and a means of resuscitation for the patient, it does not matter whether he is treated with a coagulant or not. But if it is a question of first-aid treatment and the patient is not going to reach hospital for five or six days, then a coagulant must be used, and, moreover, one which is an antiseptic. If a patient has been badly burned and is got to hospital within half an hour it does not matter whether you use sulphonamide cream, or paraffin or oil, as long as sepsis is prevented. The difficulty is in the cases which do not reach hospital for some days. Here a coagulant must be used, and the men in the destroyers must be told that above all things they must keep the patient warm.

Wing-Commander J. C. Neely said that an analysis of 120 cases of burns received at an R.A.F. hospital showed that 80% affected the face, and of this 80%, 20% had ectropion and 5% only had the globe affected. The cause of this type of burn was, of course, (1) physical, i.e. petrol flames, incendiary and flash bombs, or (2) chemical, i.e. caustic acid and alkalis and gaseous chemicals. For prophylaxis the goggles which were first issued were inadequate because of their restricted visual fields. These have been modified according to the specification of Air Commodore Livingston and now have a very wide field of vision, but still in the large bombers none of the men wear these goggles because they interfere with night vision.

[Lantern slides of the goggles used for flying and for men engaged in acetylene welding and for blacksmiths and others were shown on the screen. The pictures included a remarkable one of the amount of material which collected on the lenses and which would have entered the eye had not the protective device been worn.]

Flight-Lieutenant D. C. Bodenham said that as had been pointed out, in war burns of the face due to exposure to flame, the eyelids were very frequently involved. He stressed the importance of the sebaceous glands and hair follicles of the skin, because *in destructive burns there were invariably isolated epithelial cells left in the dermis, and it was from these island cells, by spreading and coalescing, that healing occurred.*

Two types of burn were important from the point of view of treatment, namely, the superficial second degree burn affecting the epithelium only, and the destructive or third degree burn in which all or practically all of the dermis was destroyed. But it was surprising how often epithelial islands survived and were sufficient to bring about the healing

of small areas, although in the case of extensive destruction this was much too slow and skin grafting was necessary.

He showed a typical second degree burn, saying that it would heal with very little trouble, almost without treatment, and would present practically no problem provided it was kept clean.

The real problem was the destructive third degree burn, with the epithelium hanging in loose shreds, exposing the underlying dermis, which was coagulated. No treatment would entirely prevent scarring in these cases. His lantern slides included histological pictures of the appearance of the second and third degree burn. In the latter, no cell structure was left at all. There was just one indistinguishable mass, and the skin was completely destroyed.

In facial burns, owing to the very loose supporting tissues, a tremendous amount of œdema developed even with a moderate burn. The œdema began to make its appearance a few minutes after the accident and increased up to twelve hours. It remained at the maximum from twelve to thirty-six hours and then began to subside. This had a bearing on the management of these cases, particularly of the eyes, as at this early stage it was difficult to open the eyes and therefore these patients were got into hospital under expert care as soon as possible. The Royal Air Force was fortunate in this respect and most of them were in expert hands very soon after the accident. It was remarkable how rarely the globe was involved, even in the most destructive cases.

In the Air Force they saw only a few flash burns. These burns were due to the instantaneous combustion of magnesium used in flash bombs. In these the exposure was a matter of a fraction of a second, whereas in the flame burn it was anything from 10 to 60 seconds, and that gave a chance for the closing of the eyelids, which tended to save the globe at the expense of the lid. In the flash burn, though there was conjunctival involvement the exposure was so brief that the burn was largely superficial. The globe in these cases was somewhat protected by the constant film of moisture which bathed the cornea and the conjunctiva.

In magnesium flash burns tattooing of the globe sometimes occurred, owing to minute particles being driven home by the force of the explosion. Unfortunately they were often too small and too numerous to be removed surgically. Though the skin of the eyelid was particularly delicate, it was surprising how, even in the worst burns of the eyelids, the tarsal plates remained intact.

He next showed pictures of a third degree burn taken from the fifth day onwards. In the first some œdema was still remaining, and the lids were closed on the ninth day. There were red granulations which bled easily. As shown in this case there was often ultimate scarring, with failure to close the lids completely.

Treatment.—After showing other examples of cases of burns received by airmen, the speaker turned to the question of treatment. In the Royal Air Force the results with tannic acid were so unsuccessful that quite early in the war its use was forbidden in R.A.F. and E.M.S. hospitals.

The present-day treatment rested on simple principles, namely, to prevent infection and to do as little harm as possible to the healing tissues. If infection developed it should be treated specifically. Early healing should be the aim, and if the case did not heal on its own, it should be assisted by skin grafting. For some eighteen months they had been using the synthetic detergent C.T.A.B. (cetyl trimethyl ammonium bromide) prepared by Imperial Chemical Industries. It was used in 0·75% water solution and at the same time was a very good antiseptic, seeming to combine many valuable features for the primary cleansing of fresh burns. It was applied with a swab of cotton-wool. Any loose-hanging threads of epithelium were then removed. This could be done with the aid of morphia to keep the patient quiet, not to relieve pain, because in the early stages of destructive burns there was no pain. Cleansing was followed by an application of sulphonamide either as powder or 3% cream as advocated by Dr. Colebrook. The face was covered by coarse mesh vaselin gauze, and this made a very soft, gentle non-traumatic dressing, and one which could be easily removed.

Facial burns were particularly open to infection. The nose and mouth could not be covered completely and formed an adjacent source of staphylococci and streptococci, which obtained easy access to the burnt tissue, and in this way infection, particularly with the staphylococcus, occurred almost always in the treatment of these severe burns. Penicillin had been used as a local application. If it was used in a cream base he preferred a simple mixture of lanette wax and vaselin. Penicillin made to a strength of 100 units per gramme was consistently effective in eliminating streptococci and staphylococci from granulating surfaces. It was applied every twenty-four hours, and the cases as a rule responded within four days. In undertaking specific treatment they often came

back to penicillin because of the failure of the sulphonamides, and in this way they obtained the conditions under which healing took place most rapidly.

Later when contracture of the lids developed, some degree of keratitis was not infrequent, and might go on to ulceration with loss of the eye, though this had not occurred in his experience. In the milder cases simple measures might be employed, such as constantly keeping the globe moist with saline and using a lubricant such as liquid paraffin. In the severe cases with complete ectropion developing before the face and lids had healed, this alone would not prevent keratitis. A case was shown wearing a contact lens.

Effective protection to the cornea could be given much more simply by wearing a standard anti-gas eye shield. A picture was shown with one in use on a severe case. These eye shields were particularly valuable in protecting the cornea when such cases came to operation for skin grafting of other areas.

They could be used with complete confidence and many sore eyes could be avoided by this simple measure.

Squadron Leader G. W. Cashell said that it was interesting to note that in the R.A.F. type of burns of the face it is unusual to find any burning of the cornea or conjunctiva. The lids which were instinctively closed, bore the brunt of the trauma, and in the majority of cases there was only some slight reddening of the conjunctiva, and slight œdema of the corneal epithelium.

Cases of direct burning of the conjunctiva have been due to: (1) a magnesium flash bomb; (2) incendiary bomb: (3) the effect of phosphorus; (4) concentrated sulphuric acid.

In treating cases where the conjunctiva and cornea were directly involved, the important thing was the prevention of adhesions between these two structures, or between the palpebral and ocular conjunctiva with obliteration of the fornix. It was much easier to prevent these complications than to deal with them.

Squadron Leader Cashell then gave details of five cases:

CASE I.—Flash bomb burns to Sgt. G., aged 31, Flight Engineer. While flying over enemy territory, was injured when a flash bomb exploded in the flare shoot of the aircraft. The chief effect in this case was the production of multiple fine abrasions of corneæ of both eyes, with masses of fine foreign bodies embedded in each. The burning effect in this case was very slight and the vision was 6/12 each eye. unimproved on account of the corneal nebulæ.

CASE II.—In sharp contrast was the case of L.A.C. B., aged 22, an Armourer. He was injured when a magnesium bomb exploded and had very severe burning of the corneæ in both eyes, and the eyes became badly infected. forming deep necrotic ulcers. He was transferred temporarily under the speaker's care. The chief effect in this case was the secondary infection following the burns to the cornea. The eyes became much cleaner after starting treatment with penicillin. The culture from both eyes showed *Staph. aureus.*

CASE III.—Burn from an incendiary bomb Sgt. S. of a Bomb Disposal Unit. He sustained severe burns of the lower and inner conjunctival fornix. Dense adhesions had formed between the lower lid and the globe. The lower canaliculus had been obliterated in scar tissue and the cornea was badly ulcerated. He was first treated with a Thiersch skin graft inserted in the lower fornix which took well. but was not well tolerated in association with the adjacent conjunctiva and cornea. The eye remained irritable and the conjunctiva was chronically ulcerated along the edge of the graft. which was attached to the limbus. It was decided to replace the skin with a mucous membrane graft. A large amount of mucous membrane can be obtained from the inside of the lower lip. With the help of Squadron Leader Matthews. who took the graft, the original skin graft was removed, and the mucous membrane graft inserted; this was kept in place by means of a contact lens. Although the vision in this case was very poor, on account of the extensive corneal nebulæ. the eye was comfortable and the cornea smoothly healed. The mucous membrane still looks rather red and swollen. but it may contract down, leaving an eye that is fairly comfortable and not too unsightly.

CASE IV.—Was quoted from a publication by Wing-Commander T. Keith Lyle and Squadron Leader A. G. Cross in the *British Journal of Ophthalmology*, 1942, 26, 301, where they described the delayed effect of direct burns to the eye with phosphorus. The case. R. K.. an airman, sustained burns to the eyes in 1918. and following that had frequent recurring attacks of keratitis and scleritis. The effect resembled mustard gas keratitis. but the clinical features were different. The main lesion was a scleritis with a deep corneal opacity separated from the sclera by a small ring of clear cornea. There was very little corneal vascularization. It was suggested that the condition of the cornea was a degenerative one originating with phosphorus burn.

CASE V.—Sulphuric acid burns to the face and left eye of L.A.C. D. (A full report of this case had already been made and would appear elsewhere.) This airman sustained the injury when a carboy of concentrated sulphuric acid broke and splashed him. He was admitted to hospital shortly after the accident, and in addition to burns of the hands and legs. had a burn involving the cornea and lower conjunctival fornix of left eye. The problems to be dealt with here were: (1) Control of the infection: (2) prevention of symblepharon.

The infection with the hæmolytic streptococcus was quickly controlled with penicillin, applied in the form of drops, and this materially assisted the solution of the second problem. The prevention of symblepharon was by means of a contact lens manufactured in the hospital, with the co-operation of the dental officer. Under a general anæsthetic, a cast was taken of the eye in a soft dental wax. From this was made a contact lens in portex acrylic resin. The lens was fitted within four days of the injury and worn continuously for twenty-one days. The result was excellent. The man now had a healthy mobile eye, with a small corneal nebula, and a vision of 6/9.

The points to be noted with regard to these special types of burns were: (1) Control of infection. (2) Prevention of symblepharon, which could be guaranteed by the use of rapidly made plastic contact lens. (3) Mucous membrane could be used to restore the conjunctival fornix, where obliteration had occurred, and was less irritating than skin.

Mr. T. Pomfret Kilner said that he intended to confine his contribution to the showing of a film indicating clearly the technique of eyelid grafting. This seemed all the more justifiable since a very high percentage of the repair work on burns about the eyelids is concerned with the treatment of ectropion.

During the projection of the film he advised that when possible only one eyelid should be tackled at a time: that it was unwise to graft upper and lower eyelids at the same operation, for if this was attempted it was difficult to obtain over-correction on which success so much depended: that approximation of eyelids by tarsorrhaphy and grafting both eyelids with a single mould-applied graft failed to give the necessary area of new skin, re-eversion of the eyelid over the mould being essential.

He also stressed (*a*) the importance of early grafting—even at the risk of recontracture or partial failure—to provide covering for an exposed cornea and avoidance of ulceration and opacity formation. (*b*) The need to remember the bearing of other scarred areas of the face on the eyelids—release of scarring of the cheek or forehead regions often being needed to overcome drag on the eyelids. (*c*) The importance of diagnosing the extent and type of loss, it being useless trying to repair full-thickness loss by free skin grafting.

He hoped that he was passing on information from his experience which would help surgeons to deal with such cases as were under consideration when the services of a plastic specialist were not available.

Mr. Frederick Ridley spoke of the protection of the eye. His observations were based upon the experience of a Maxillo-Facial Unit, where more than 100 cases of burns so severe as to require lid-grafting had been treated. They were summarized as follows:

No coagulants should be used in the treatment of the eyelids; the splinting effect, the difficulty of proper care of the eye, the discomfort and the fact that nothing is gained by waterproofing such a minute area are strong contra-indications.

Tulle gras dressings and saline packs are satisfactory. The full saline bath has a dramatic effect in alleviating blepharospasm and photophobia. Argyrol 10% b.d. and atropine 1% daily protect against local sepsis and anticipate the development of corneal mischief. Organic silver preparations used should be neutral, many are strongly alkaline.

Grafting of the lids should be undertaken as soon as lid retraction develops. Healing is promoted and such grafts do better than expected. Burnt areas remote from the lids contribute much to the retraction and should be grafted as soon as possible.

Only four cases had failed to respond to this routine. Two developed ulceration with some visual loss. This experience led to the use of mechanical protection in the other two cases.

The exposed cornea may be protected by contact lenses; delay in production, discontinuity of wearing, retention of pus, and discomfort are serious disadvantages. Lid suture is impracticable in the acute septic stage and useless in the cicatricial stage. Early cases with loss of lid tissue may be saved by sliding down a frontal skin flap and suturing over the exposed eye. If an unburnt skin area is available an acrylic mask should be worn. This should be moulded from a cast of the face and should fit both the face and the eye perfectly. The part apposed to the eye itself should be lined with thin sheet dental casting wax. Against this the cornea moves with comfort and retains its polish. A narrow tube may be built into the centre of the mask to facilitate irrigation of the eye. A solution of 10% of the patient's serum in 0·5% saline reproduces the surface tension of the tears and wets the cornea perfectly. Atropine or other drugs may be added. If a mask cannot be worn a small shield filling the palpebral aperture may be fitted, as was described in the *Brit. Med. J.*, 1943 (ii), 268. This shield is carried on an extension bar from a dental cap splint.

Two Cases of Whole-Thickness Skin Grafts to the Lower Lid.—Major A. SEYMOUR PHILPS, R.A.M.C. (for Sir HAROLD GILLIES, C.B.E., F.R.C.S.).

Both patients had had whole-thickness skin grafts to the lower lid taken from behind the ear. Attention was drawn to the good colour match of this skin with the surrounding area. It was much better than that usually obtained with a Thiersch graft.

Flying-Officer K. was shot down over Tripoli and captured by the Italians. He was badly burned about the face and hands, and by the time he was repatriated there was marked scarring and ectropion of the lower lids of both eyes. He has now had both lower lids grafted (May 1943) and also nose (August 1943).

The second patient, a hospital porter, though *not* injured by burning, had a marked degree of cicatricial ectropion of the right lower lid. This was grafted in August 1943, and although two months had not yet elapsed the result appeared to be very satisfactory.

Metallic Foreign Body in the Vitreous.—VIOLET M. ATTENBOROUGH, D.O.M.S. (for T. C. SUMMERS, F.R.C.S.).

T. C., male, aged 37. Riveter.

The patient was first seen in March 1943.

He gave a history of having received an injury to the right eye a year before whilst riveting duralumin. Vision in the right eye was then 6/9, in the left eye 6/6. A large foreign body could be seen projecting into the vitreous. This proved to be non-magnetic. The eye was quiet. In September the patient complained that his right vision was failing.

Vision in right eye is now 6/24. The vitreous is hazy and there are metallic deposits on the surface of and in the lens capsule. There is a greenish coloration throughout the whole of the lens.

The left eye is unaffected.

Other cases were shown as follows:

Tarsectomy for Intractable Trachoma.—A. F. MACCALLAN, C.B.E., F.R.C.S.

Bilateral Hæmorrhagic Retinitis with Retinal Detachments.—VIOLET M. ATTENBOROUGH, D.O.M.S.

(1) **Anophthalmos Following Injury Where Artificial Eye Had Not Been Removed From Socket For 27 Years.** (2) **Congenital Pigmentation of Right Nerve-Head, Vision Being Unaffected.**—V. B. PURVIS, M.B.

Clinical Section

President—J. D. ROLLESTON, M.D.

[*October* 8, 1943]

The Clinical Society of London (1868-1907)

PRESIDENT'S ADDRESS

By J. D. ROLLESTON, M.D.

IN contrast with the practice of the parent society on only two previous occasions have Presidential Addresses been given before the Clinical Section. One was that of Sir Thomas Barlow in 1907, which was the first to be delivered before the Section after the Clinical Society became merged in the Royal Society of Medicine, while the other was Sir Anthony Bowlby's Address in 1920 "On the Application of War Methods to Civil Practice."

A proposal to make a Section of Clinical Medicine and Surgery as well as of other subjects, part of a Royal Society of Medicine dates back to 1868, when a committee to deal with the matter was set up by the Royal Medical and Chirurgical Society and was further discussed the following year, but nothing came of it (Moore and Paget, 1905).

In 1892 Sir Andrew Clark, who was president of that Society, raised the question of amalgamation again, but died before much progress was made in effecting union, and his successor Mr., afterwards Sir, Jonathan Hutchinson was so opposed to it that the matter was not resuscitated until 1905, when a revised scheme of union was made and two years later the union of the Royal Medical and Chirurgical Society with seventeen other *Societies* was firmly established.

The term "Clinical Society of London" has been erroneously applied in the First Series of the Surgeon-General's Catalogue, 1882, 229, to a Clinical Society at Guy's Hospital founded in 1836, also called "Clinical Report Society", whose proceedings were incorporated for many years in *Guy's Hospital Reports*.

According to James Blake Bailey, librarian of the Royal College of Surgeons, the formation of the Clinical Society of London, *the parent* of the Clinical Section of the Royal Society of Medicine, was mainly due to Dr. Headlam Greenhow and Dr., afterwards Sir, John Burdon Sanderson, who were both assistant physicians to the Middlesex Hospital, the latter subsequently going to Oxford where he was appointed first Waynflete Professor of Physiology and later Regius Professor of Medicine. According to Sir John Bland-Sutton Greenhow's only monument consists of specimens illustrating Addison's disease and miner's phthisis in the Museum of the Middlesex Hospital, but he was also the author of the best pre-antitoxin work on diphtheria and *also* of a valuable monograph on Addison's disease. On October 29, 1867, a meeting was held at Burdon Sanderson's house, 49, Queen Anne Street, with Greenhow in the Chair, to discuss the formation of a Society "for the cultivation and promotion of practical medicine and surgery by the collection of cases, especially such as bear upon undetermined questions in pathology and therapeutics." A provisional committee was then appointed, and a sub-committee consisting of Dr., afterwards Sir, George Buchanan, Medical Inspector to the Privy Council, Mr. Callender, assistant surgeon to St. Bartholomew's Hospital, Dr. Greenhow, Dr. Sydney Ringer, physician to University College Hospital and Dr. Burdon Sanderson, *was nominated* to prepare a draft of rules for the Society. The proposal met with immediate *success*. At a meeting on December 9, 1867, it was reported that 110 original members had joined the Society. Sir Thomas Watson, the leading physician of the day, indeed it has been said of the century, as well as author of a classical work on "The Principles and Practice of Physic," was appointed first President with Dr. Burdon Sanderson and Mr. Callender as the first Secretaries. The first General Meeting was held on January 10, 1868, when Sir Thomas Watson delivered his Presidential Address. With the exception of the first session which was held from January to May, all the sessions were held from October to May, as in the Clinical Section to-day, but took place twice a month, namely on the second and fourth Fridays.

The business of each Ordinary Meeting consisted in the receiving of communications of two classes; the first relating to cases of which the records were complete, while those of the second class were still under observation. No communication was to exceed ten minutes, longer papers being regarded as more suitable for the Royal Medical and Chirurgical Society. Annual Meetings were held for the election of officers and other members of the Council, and Special Meetings were convened by the President and Council for the consideration of special business The meetings were successively held at 53, Berners Street in the rooms of the Royal Medical and Chirurgical Society, at 33,

DEC.—CLIN. 1

George Street, Hanover Square, in the rooms of the Medical Society of London, and again in the rooms of the Royal Medical and Chirurgical Society at 20, Hanover Square.

Cases shown were drawn from all departments of medicine in the widest sense of the word. Dermatology was represented by Radcliffe Crocker, Colcott Fox, Tilbury Fox, Malcolm Morris, and J. J. Pringle; Epidemiology by George Buchanan and Sir Richard Thorne-Thorne; Neurology by Charlton Bastian, C. E. Beevor, Thomas Buzzard, Sir William Gowers and Hughlings Jackson; Ophthalmology by E. Nettleship, George Lawson and Brudenell Carter; Orthopædics by J. Jackson Clarke, T. H. Openshaw and Bernard Roth; Otorhinolaryngology by Sir Felix Semon, Sir Morell Mackenzie and Sir William Dalby; Pædiatrics by Sir Thomas Barlow, J. F. Goodhart and Sir G. F. Still, and Urology by Sir Henry Thompson, Sir George Buckston Browne, W. F. Teevan, Hurry Fenwick and David Newman. As regards my own speciality of acute infectious diseases, the *Transactions* of the Clinical Society show that this subject received much more attention than it subsequently did at the Clinical Section, as is seen from the fact that during the forty years of the Clinical Society's existence there were some fifty cases of acute infectious disease recorded, particularly diphtheria, scarlet fever and typhoid, as compared with only fifteen in the *Transactions* of the Clinical Section between 1907 and 1942.

Undoubtedly the most interesting historical event connected with the Clinical Society was the first medical demonstration held in this country of X-rays nearly fifty years ago. Sir William Hale-White, who was honorary secretary at the time, said: "Early in 1896 the Society invited Professor Sylvanus Thompson, the celebrated physicist, to tell its members about the new discovery. A Special Meeting was held on March 30, 1896, in the Society's rooms in Hanover Square and was attended by nearly 400 members." As the professor did not read a formal paper, the demonstration was not recorded in the *Transactions*, but short notices of the event appeared in the *Lancet* (1896, i, 935) and *British Medical Journal* (1896, i, 875) at the time. Subsequently numerous cases illustrating the diagnostic and therapeutic value of X-rays were reported at the meetings of the Society, and recorded in Volumes 30 to 40 of its *Transactions*.

At the time of its amalgamation in the Royal Society of Medicine in 1907 the Clinical Society numbered 572 ordinary members and 16 honorary members, seven of whom were British, viz. Sir William Broadbent, Thomas Bryant, Lord Lister, Sir William Osler, Sir Thomas Smith and Sir Samuel Wilks, and nine foreign, namely John Billings, Wilhelm Erb, Friedrich von Esmarch, William Williams Keen, Theodor Kocher, Ernst von Leyden, Just Lucas-Championnière, Costanzo Mazzoni and Weir Mitchell.

Sir Thomas Watson was the first and most eminent President of the Clinical Society, of whom John Marshall in his Presidential Address before the Royal Medical and Chirurgical Society, of which Watson was a Vice-President, said: "All his titles must yield in significance to that of being termed 'the greatest English Physician of the present century,' a designation which he fairly earned by his professional eminence, his moral worth, his sagacity, his integrity, his undeviating regard for the feelings and interests of his brethren, and by his steady adhesion to those high principles of duty, which he so eloquently expounded in his well-known and often quoted 'Introductory Lecture,' and which made him so fit an adviser on ethical questions relating to our profession." (*See* my paper entitled "Sir Thomas Watson, President, Royal College of Physicians," to appear in a forthcoming number of *The Medical Press and Circular*.)

Of the 19 other Presidents of the Society the most notable were Sir William Broadbent, Sir Douglas Powell and Sir Frederick Taylor among the physicians, and Sir James Paget, Lord Lister, Thomas Bryant, Howard Marsh and Hugh Clutton among the surgeons.

The rules of the Society ordained that each President should hold office for two years and that surgeons should alternate with physicians—a rule which was and still is rigidly observed. Each President either in his first or second year of office delivered an Address—a rule which was also faithfully kept by the Society though not subsequently by the Section. Four Presidents indeed, viz. Dr. Greenhow, Sir William Gull, Sir Dyce Duckworth and Sir Prescott Hewitt gave two Addresses, the first being Inaugural and the second Valedictory. The great majority of Presidential Addresses dealt with generalities, and only three had definite titles, viz. those by Sir Prescott Gardiner Hewitt on Pyæmia in General Practice (*Trans. clin. Soc. Lond.*, 7, 1874), Joseph Lister, as he was then, on The Catgut Ligature (12, 1881), and H. H. Clutton on Adolescent or Late Rickets (39, 1907).

A remarkable custom in the practice of the Society, which, doubtless, owing to life having become much more strenuous, is not now observed by the Section, was the frequent formation of special committees to discuss various subjects or individual cases. Of such committees undoubtedly the three most important were those on myxœdema (21, *Suppl.*), the periods of incubation and contagiousness of certain infectious diseases (25, *Suppl.*) and the antitoxin of diphtheria (31 *End*), of which the members were Dr. W. S. Church, Stephen Mackenzie, Sidney Coupland, Hale-White, Sidney Ringer, William Pasteur (Hon. Sec.), J. W. Washbourn, H. P. Hawkins and last but by no means least, E. W. Goodall (31, 1898). Other interesting subjects discussed by special committees

were The Temperature in Syphilis (3, 1870, 170), Hyperpyrexia in Rheumatism (1882, 15, 261), Excision of Hip-joint (1881, 14, 223) and Joint Disease and Locomotor Ataxia (20, 1887, 271). Reference should also be made to the Supplement (22, 1889) containing additional information concerning the cases reported in the first 21 volumes of the *Transactions* and compiled by a committee of five physicians and five surgeons appointed by the Council at the suggestion of the President, Mr. Christopher Heath.

George Richmond. R.A. pinx.   *S. Cousins, sculp.*

SIR THOMAS WATSON, BART.

The financial position of the Society was eminently satisfactory throughout its course and this is no doubt to be attributed to the business capacity of the treasurers, three of whom—Greenhow, Heath and Ord—held office for ten or eleven successive years. The largest sum expended by the Society at one time was £300 for the publication of the Committee's Report on Myxœdema, £100 of which, however, was defrayed by Dr. W. M. Ord, the Chairman of the Committee.

No account of the activities of the Clinical Society would be complete without allusion to the valuable author and subject indexes of the *Transactions*, occupying two volumes. The first, which was compiled by Dr., afterwards Sir, Archibald E. Garrod, appeared in 1898, and dealt with the thirty years 1868-1897, while the second published in 1919 covered the period 1898-1907.

REFERENCES

BAILEY, J. B. (1895) *Brit. Med. J.* (ii), 102.
BLAND-SUTTON, Sir J. (1930) " The Story of a Surgeon," 59. London.
HALE-WHITE, W. (1930) *Lancet* (ii), 1370.
MARSHALL, J. (1883) *Med. Chir. Trans.*, 66, 27.
MOORE, N., and PAGET, S. (1905) The Royal Medical and Chirurgical Society of London Centenary. Centenary, 136.
ROLLESTON, J. D. (1924-25) *Proc. R. Soc. Med.*, 18 (Sect. Hist. Med., 1).
—— (1926-27) *Proc. R. Soc. Med.*, 20 (Child. Sect., 55).
—— (1933-34) *Proc. R. Soc. Med.*, 27, 177.

Carcinoma of Œsophagus: Resection and Œsophago-gastrostomy.—VERNON C. THOMPSON, F.R.C.S.

J. W., aged 53, Labourer.

History.—June 1941: Sudden onset of dysphagia. September 1941: Carcinoma of œsophagus diagnosed by X-ray.

George Street, Hanover Square, in the rooms of the Medical Society of London, and again in the rooms of the Royal Medical and Chirurgical Society at 20, Hanover Square.

Cases shown were drawn from all departments of medicine in the widest sense of the word. Dermatology was represented by Radcliffe Crocker, Colcott Fox, Tilbury Fox, Malcolm Morris, and J. J. Pringle; Epidemiology by George Buchanan and Sir Richard Thorne-Thorne; Neurology by Charlton Bastian, C. E. Beevor, Thomas Buzzard, Sir William Gowers and Hughlings Jackson; Ophthalmology by E. Nettleship, George Lawson and Brudenell Carter; Orthopaedics by J. Jackson Clarke, T. H. Openshaw and Bernard Roth; Otorhinolaryngology by Sir Felix Semon, Sir Morell Mackenzie and Sir William Dalby; Pædiatrics by Sir Thomas Barlow, J. F. Goodhart and Sir G. F. Still, and Urology by Sir Henry Thompson, Sir George Buckston Browne, W. F. Teevan, Hurry Fenwick and David Newman. As regards my own speciality of acute infectious diseases, the *Transactions* of the Clinical Society show that this subject received much more attention than it subsequently did at the Clinical Section, as is seen from the fact that during the forty years of the Clinical Society's existence there were some fifty cases of acute infectious disease recorded, particularly diphtheria, scarlet fever and typhoid, as compared with only fifteen in the *Transactions* of the Clinical Section between 1907 and 1942.

Undoubtedly the most interesting historical event connected with the Clinical Society was the first medical demonstration held in this country of X-rays nearly fifty years ago. Sir William Hale-White, who was honorary secretary at the time, said: "Early in 1896 the Society invited Professor Sylvanus Thompson, the celebrated physicist, to tell its members about the new discovery. A Special Meeting was held on March 30, 1896, in the Society's rooms in Hanover Square and was attended by nearly 400 members." As the professor did not read a formal paper, the demonstration was not recorded in the *Transactions*, but short notices of the event appeared in the *Lancet* (1896, i, 935) and *British Medical Journal* (1896, i, 875) at the time. Subsequently numerous cases illustrating the diagnostic and therapeutic value of X-rays were reported at the meetings of the Society, and recorded in Volumes 30 to 40 of its *Transactions*.

At the time of its amalgamation in the Royal Society of Medicine in 1907 the Clinical Society numbered 572 ordinary members and 16 honorary members, seven of whom were British, viz. Sir William Broadbent, Thomas Bryant, Lord Lister, Sir William Osler, Sir Thomas Smith and Sir Samuel Wilks, and nine foreign, namely John Billings, Wilhelm Erb, Friedrich von Esmarch, William Williams Keen, Theodor Kocher, Ernst von Leyden, Just Lucas-Championnière, Costanzo Mazzoni and Weir Mitchell.

Sir Thomas Watson was the first and most eminent President of the Clinical Society, of whom John Marshall in his Presidential Address before the Royal Medical and Chirurgical Society, of which Watson was a Vice-President, said: "All his titles must yield in significance to that of being termed 'the greatest English Physician of the present century,' a designation which he fairly earned by his professional eminence, his moral worth, his sagacity, his integrity, his undeviating regard for the feelings and interests of his brethren, and by his steady adhesion to those high principles of duty, which he so eloquently expounded in his well-known and often quoted 'Introductory Lecture,' and which made him so fit an adviser on ethical questions relating to our profession." (*See* my paper entitled "Sir Thomas Watson, President, Royal College of Physicians," to appear in a forthcoming number of *The Medical Press and Circular*.)

Of the 19 other Presidents of the Society the most notable were Sir William Broadbent, Sir Douglas Powell and Sir Frederick Taylor among the physicians, and Sir James Paget, Lord Lister, Thomas Bryant, Howard Marsh and Hugh Clutton among the surgeons.

The rules of the Society ordained that each President should hold office for two years and that surgeons should alternate with physicians—a rule which was and still is rigidly observed. Each President either in his first or second year of office delivered an Address—a rule which was also faithfully kept by the Society though not subsequently by the Section. Four Presidents indeed, viz. Dr. Greenhow, Sir William Gull, Sir Dyce Duckworth and Sir Prescott Hewitt gave two Addresses, the first being Inaugural and the second Valedictory. The great majority of Presidential Addresses dealt with generalities, and only three had definite titles, viz. those by Sir Prescott Gardner Hewitt on Pyæmia in General Practice (*Trans. clin. Soc. Lond.,* 7, 1874), Joseph Lister, as he was then, on The Catgut Ligature (12, 1881), and H. H. Clutton on Adolescent or Late Rickets (39, 1907).

A remarkable custom in the practice of the Society, which, doubtless, owing to life having become much more strenuous, is not now observed by the Section, was the frequent formation of special committees to discuss various subjects or individual cases. Of such committees undoubtedly the three most important were those on myxœdema (21, *Suppl.*), the periods of incubation and contagiousness of certain infectious diseases (25, *Suppl.*) and the antitoxin of diphtheria (31 *End*), of which the members were Dr. W. S. Church, Stephen Mackenzie, Sidney Coupland, Hale-White, Sidney Ringer, William Pasteur (Hon. Sec.), J. W. Washbourn, H. P. Hawkins and last but by no means least, E. W. Goodall (31, 1898). Other interesting subjects discussed by special committees

were The Temperature in Syphilis (3, 1870, 170), Hyperpyrexia in Rheumatism (1882, 15, 261), Excision of Hip-joint (1881, 14, 223) and Joint Disease and Locomotor Ataxia (20, 1887, 271). Reference should also be made to the Supplement (22, 1889) containing additional information concerning the cases reported in the first 21 volumes of the *Transactions* and compiled by a committee of five physicians and five surgeons appointed by the Council at the suggestion of the President, Mr. Christopher Heath.

George Richmond, R.A. pinx.   *S. Cousins, sculp.*

SIR THOMAS WATSON, BART.

The financial position of the Society was eminently satisfactory throughout its course and this is no doubt to be attributed to the business capacity of the treasurers, three of whom—Greenhow, Heath and Ord—held office for ten or eleven successive years. The largest sum expended by the Society at one time was £300 for the publication of the Committee's Report on Myxœdema, £100 of which, however, was defrayed by Dr. W. M. Ord, the Chairman of the Committee.

No account of the activities of the Clinical Society would be complete without allusion to the valuable author and subject indexes of the *Transactions*, occupying two volumes. The first, which was compiled by Dr., afterwards Sir, Archibald E. Garrod, appeared in 1898, and dealt with the thirty years 1868-1897, while the second published in 1919 covered the period 1898-1907.

REFERENCES

BAILEY, J. B. (1895) *Brit. Med. J.* (ii), 102.
BLAND-SUTTON, Sir J. (1930) " The Story of a Surgeon," 59. London.
HALE-WHITE, W. (1930) *Lancet* (ii), 1370.
MARSHALL, J. (1883) *Med. Chir. Trans.*, 66, 27.
MOORE, N., and PAGET, S. (1905) The Royal Medical and Chirurgical Society of London Centenary. Centenary, 136.
ROLLESTON, J. D. (1924-25) *Proc. R. Soc. Med.*, 18 (Sect. Hist. Med., 1).
—— (1926-27) *Proc. R. Soc. Med.*, 20 (Child. Sect., 55).
—— (1933-34) *Proc. R. Soc. Med.*, 27, 177.

Carcinoma of Œsophagus: Resection and Œsophago-gastrostomy.—VERNON C. THOMPSON, F.R.C.S.

J. W., aged 53, Labourer.

History.—June 1941: Sudden onset of dysphagia. September 1941: Carcinoma of œsophagus diagnosed by X-ray.

George Street, Hanover Square, in the rooms of the Medical Society of London, and again in the rooms of the Royal Medical and Chirurgical Society at 20, Hanover Square.

Cases shown were drawn from all departments of medicine in the widest sense of the word. Dermatology was represented by Radcliffe Crocker, Colcott Fox, Tilbury Fox, Malcolm Morris, and J. J. Pringle; Epidemiology by George Buchanan and Sir Richard Thorne-Thorne; Neurology by Charlton Bastian, C. E. Beevor, Thomas Buzzard, Sir William Gowers and Hughlings Jackson; Ophthalmology by E. Nettleship, George Lawson and Brudenell Carter; Orthopædics by J. Jackson Clarke, T. H. Openshaw and Bernard Roth; Otorhinolaryngology by Sir Felix Semon, Sir Morell Mackenzie and Sir William Dalby; Pædiatrics by Sir Thomas Barlow, J. F. Goodhart and Sir G. F. Still, and Urology by Sir Henry Thompson, Sir George Buckston Browne, W. F. Teevan, Hurry Fenwick and David Newman. As regards my own speciality of acute infectious diseases, the *Transactions* of the Clinical Society show that this subject received much more attention than it subsequently did at the Clinical Section, as is seen from the fact that during the forty years of the Clinical Society's existence there were some fifty cases of acute infectious disease recorded, particularly diphtheria, scarlet fever and typhoid, as compared with only fifteen in the *Transactions* of the Clinical Section between 1907 and 1942.

Undoubtedly the most interesting historical event connected with the Clinical Society was the first medical demonstration held in this country of X-rays nearly fifty years ago. Sir William Hale-White, who was honorary secretary at the time, said: "Early in 1896 the Society invited Professor Sylvanus Thompson, the celebrated physicist, to tell its members about the new discovery. A Special Meeting was held on March 30, 1896, in the Society's rooms in Hanover Square and was attended by nearly 400 members." As the professor did not read a formal paper, the demonstration was not recorded in the *Transactions*, but short notices of the event appeared in the *Lancet* (1896, i, 935) and *British Medical Journal* (1896, i, 875) at the time. Subsequently numerous cases illustrating the diagnostic and therapeutic value of X-rays were reported at the meetings of the Society, and recorded in Volumes 30 to 40 of its *Transactions*.

At the time of its amalgamation in the Royal Society of Medicine in 1907 the Clinical Society numbered 572 ordinary members and 16 honorary members, seven of whom were British, viz. Sir William Broadbent, Thomas Bryant, Lord Lister, Sir William Osler, Sir Thomas Smith and Sir Samuel Wilks, and nine foreign, namely John Billings, Wilhelm Erb, Friedrich von Esmarch, William Williams Keen, Theodor Kocher, Ernst von Leyden, Just Lucas-Championnière, Costanzo Mazzoni and Weir Mitchell.

Sir Thomas Watson was the first and most eminent President of the Clinical Society, of whom John Marshall in his Presidential Address before the Royal Medical and Chirurgical Society, of which Watson was a Vice-President, said: "All his titles must yield in significance to that of being termed 'the greatest English Physician of the present century,' a designation which he fairly earned by his professional eminence, his moral worth, his sagacity, his integrity, his undeviating regard for the feelings and interests of his brethren, and by his steady adhesion to those high principles of duty, which he so eloquently expounded in his well-known and often quoted 'Introductory Lecture,' and which made him so fit an adviser on ethical questions relating to our profession." (*See* my paper entitled "Sir Thomas Watson, President, Royal College of Physicians," to appear in a forthcoming number of *The Medical Press and Circular*.)

Of the 19 other Presidents of the Society the most notable were Sir William Broadbent, Sir Douglas Powell and Sir Frederick Taylor among the physicians, and Sir James Paget, Lord Lister, Thomas Bryant, Howard Marsh and Hugh Clutton among the surgeons.

The rules of the Society ordained that each President should hold office for two years and that surgeons should alternate with physicians—a rule which was and still is rigidly observed. Each President either in his first or second year of office delivered an Address— a rule which was also faithfully kept by the Society though not subsequently by the Section. Four Presidents indeed, viz. Dr. Greenhow, Sir William Gull, Sir Dyce Duckworth and Sir Prescott Hewitt gave two Addresses, the first being Inaugural and the second Valedictory. The great majority of Presidential Addresses dealt with generalities, and only three had definite titles, viz. those by Sir Prescott Gardner Hewitt on Pyæmia in General Practice (*Trans. clin. Soc. Lond.*, 7, 1874), Joseph Lister, as he was then, on The Catgut Ligature (12, 1881), and H. H. Clutton on Adolescent or Late Rickets (39, 1907).

A remarkable custom in the practice of the Society, which, doubtless, owing to life having become much more strenuous, is not now observed by the Section, was the frequent formation of special committees to discuss various subjects or individual cases. Of such committees undoubtedly the three most important were those on myxœdema (21, *Suppl.*), the periods of incubation and contagiousness of certain infectious diseases (25, *Suppl.*) and the antitoxin of diphtheria (31 *End*), of which the members were Dr. W. S. Church, Stephen Mackenzie, Sidney Coupland, Hale-White, Sidney Ringer, William Pasteur (Hon. Sec.), J. W. Washbourn, H. P. Hawkins and last but by no means least, E. W. Goodall (31, 1898). Other interesting subjects discussed by special committees

were The Temperature in Syphilis (3, 1870, 170), Hyperpyrexia in Rheumatism (1882, 15, 261), Excision of Hip-joint (1881, 14, 223) and Joint Disease and Locomotor Ataxia (20, 1887, 271). Reference should also be made to the Supplement (22, 1889) containing additional information concerning the cases reported in the first 21 volumes of the *Transactions* and compiled by a committee of five physicians and five surgeons appointed by the Council at the suggestion of the President, Mr. Christopher Heath.

George Richmond, R.A. pinx.   *S. Cousins, sculp.*

SIR THOMAS WATSON, BART.

The financial position of the Society was eminently satisfactory throughout its course and this is no doubt to be attributed to the business capacity of the treasurers, three of whom—Greenhow, Heath and Ord—held office for ten or eleven successive years. The largest sum expended by the Society at one time was £300 for the publication of the Committee's Report on Myxœdema, £100 of which, however, was defrayed by Dr. W. M. Ord, the Chairman of the Committee.

No account of the activities of the Clinical Society would be complete without allusion to the valuable author and subject indexes of the *Transactions*, occupying two volumes. The first, which was compiled by Dr., afterwards Sir, Archibald E. Garrod, appeared in 1898, and dealt with the thirty years 1868-1897, while the second published in 1919 covered the period 1898-1907.

REFERENCES

BAILEY, J. B. (1895) *Brit. Med. J.* (ii), 102.
BLAND-SUTTON, Sir J. (1930) " The Story of a Surgeon," 59. London.
HALE-WHITE, W. (1930) *Lancet* (ii), 1370.
MARSHALL, J. (1883) *Med. Chir. Trans.*, 66, 27.
MOORE, N., and PAGET, S. (1905) The Royal Medical and Chirurgical Society of London Centenary. Centenary, 136.
ROLLESTON, J. D. (1924-25) *Proc. R. Soc. Med.*, 18 (Sect. Hist. Med., 1).
———   (1926-27) *Proc. R. Soc. Med.*, 20 (Child. Sect., 55).
———   (1933-34) *Proc. R. Soc. Med.*, 27, 177.

Carcinoma of Œsophagus: Resection and Œsophago-gastrostomy.—VERNON C. THOMPSON, F.R.C.S.

J. W., aged 53, Labourer.

History.—June 1941: Sudden onset of dysphagia. September 1941: Carcinoma of œsophagus diagnosed by X-ray.

George Street, Hanover Square, in the rooms of the Medical Society of London, and again in the rooms of the Royal Medical and Chirurgical Society at 20, Hanover Square.

Cases shown were drawn from all departments of medicine in the widest sense of the word. Dermatology was represented by Radcliffe Crocker, Colcott Fox, Tilbury Fox, Malcolm Morris, and J. J. Pringle; Epidemiology by George Buchanan and Sir Richard Thorne-Thorne; Neurology by Charlton Bastian, C. E. Beevor, Thomas Buzzard, Sir William Gowers and Hughlings Jackson; Ophthalmology by E. Nettleship, George Lawson and Brudenell Carter; Orthopaedics by J. Jackson Clarke, T. H. Openshaw and Bernard Roth; Otorhinolaryngology by Sir Felix Semon, Sir Morell Mackenzie and Sir William Dalby; Pædiatrics by Sir Thomas Barlow, J. F. Goodhart and Sir G. F. Still, and Urology by Sir Henry Thompson, Sir George Buckston Browne, W. F. Teevan, Hurry Fenwick and David Newman. As regards my own speciality of acute infectious diseases, the *Transactions* of the Clinical Society show that this subject received much more attention than it subsequently did at the Clinical Section, as is seen from the fact that during the forty years of the Clinical Society's existence there were some fifty cases of acute infectious disease recorded, particularly diphtheria, scarlet fever and typhoid, as compared with only fifteen in the *Transactions* of the Clinical Section between 1907 and 1942.

Undoubtedly the most interesting historical event connected with the Clinical Society was the first medical demonstration held in this country of X-rays nearly fifty years ago. Sir William Hale-White, who was honorary secretary at the time, said: "Early in 1896 the Society invited Professor Sylvanus Thompson, the celebrated physicist, to tell its members about the new discovery. A Special Meeting was held on March 30, 1896, in the Society's rooms in Hanover Square and was attended by nearly 400 members." As the professor did not read a formal paper, the demonstration was not recorded in the *Transactions*, but short notices of the event appeared in the *Lancet* (1896, i, 935) and *British Medical Journal* (1896, i, 875) at the time. Subsequently numerous cases illustrating the diagnostic and therapeutic value of X-rays were reported at the meetings of the Society, and recorded in Volumes 30 to 40 of its *Transactions*.

At the time of its amalgamation in the Royal Society of Medicine in 1907 the Clinical Society numbered 572 ordinary members and 16 honorary members, seven of whom were British, viz. Sir William Broadbent, Thomas Bryant, Lord Lister, Sir William Osler, Sir Thomas Smith and Sir Samuel Wilks, and nine foreign, namely John Billings, Wilhelm Erb, Friedrich von Esmarch, William Williams Keen, Theodor Kocher, Ernst von Leyden, Just Lucas-Championnière, Costanzo Mazzoni and Weir Mitchell.

Sir Thomas Watson was the first and most eminent President of the Clinical Society, of whom John Marshall in his Presidential Address before the Royal Medical and Chirurgical Society, of which Watson was a Vice-President, said: "All his titles must yield in significance to that of being termed 'the greatest English Physician of the present century,' a designation which he fairly earned by his professional eminence, his moral worth, his sagacity, his integrity, his undeviating regard for the feelings and interests of his brethren, and by his steady adhesion to those high principles of duty, which he so eloquently expounded in his well-known and often quoted 'Introductory Lecture,' and which made him so fit an adviser on ethical questions relating to our profession." (*See* my paper entitled "Sir Thomas Watson, President, Royal College of Physicians," to appear in a forthcoming number of *The Medical Press and Circular*.)

Of the 19 other Presidents of the Society the most notable were Sir William Broadbent, Sir Douglas Powell and Sir Frederick Taylor among the physicians, and Sir James Paget, Lord Lister, Thomas Bryant, Howard Marsh and Hugh Clutton among the surgeons.

The rules of the Society ordained that each President should hold office for two years and that surgeons should alternate with physicians—a rule which was and still is rigidly observed. Each President either in his first or second year of office delivered an Address—a rule which was also faithfully kept by the Society though not subsequently by the Section. Four Presidents indeed, viz. Dr. Greenhow, Sir William Gull, Sir Dyce Duckworth and Sir Prescott Hewitt gave two Addresses, the first being Inaugural and the second Valedictory. The great majority of Presidential Addresses dealt with generalities, and only three had definite titles, viz. those by Sir Prescott Gardner Hewitt on Pyæmia in General Practice (*Trans. clin. Soc. Lond.,* 7, 1874), Joseph Lister, as he was then, on The Catgut Ligature (12, 1881), and H. H. Clutton on Adolescent or Late Rickets (39, 1907).

A remarkable custom in the practice of the Society, which, doubtless, owing to life having become much more strenuous, is not now observed by the Section, was the frequent formation of special committees to discuss various subjects or individual cases. Of such committees undoubtedly the three most important were those on myxœdema (21, *Suppl.*), the periods of incubation and contagiousness of certain infectious diseases (25, *Suppl.*) and the antitoxin of diphtheria (31 *End*), of which the members were Dr. W. S. Church, Stephen Mackenzie, Sidney Coupland, Hale-White, Sidney Ringer, William Pasteur (Hon. Sec.), J. W. Washbourn, H. P. Hawkins and last but by no means least, E. W. Goodall (31, 1898). Other interesting subjects discussed by special committees

were The Temperature in Syphilis (3, 1870, 170), Hyperpyrexia in Rheumatism (1882, 15, 261), Excision of Hip-joint (1881, 14, 223) and Joint Disease and Locomotor Ataxia (20, 1887, 271). Reference should also be made to the Supplement (22, 1889) containing additional information concerning the cases reported in the first 21 volumes of the *Transactions* and compiled by a committee of five physicians and five surgeons appointed by the Council at the suggestion of the President, Mr. Christopher Heath.

George Richmond, R.A. pinx.   *S. Cousins, sculp.*

SIR THOMAS WATSON, BART.

The financial position of the Society was eminently satisfactory throughout its course and this is no doubt to be attributed to the business capacity of the treasurers, three of whom—Greenhow, Heath and Ord—held office for ten or eleven successive years. The largest sum expended by the Society at one time was £300 for the publication of the Committee's Report on Myxœdema, £100 of which, however, was defrayed by Dr. W. M. Ord, the Chairman of the Committee.

No account of the activities of the Clinical Society would be complete without allusion to the valuable author and subject indexes of the *Transactions*, occupying two volumes. The first, which was compiled by Dr., afterwards Sir, Archibald E. Garrod, appeared in 1898, and dealt with the thirty years 1868-1897, while the second published in 1919 covered the period 1898-1907.

REFERENCES

BAILEY, J. B. (1895) *Brit. Med. J.* (ii), 102.
BLAND-SUTTON, Sir J. (1930) " The Story of a Surgeon," 59. London.
HALE-WHITE, W. (1930) *Lancet* (ii), 1370.
MARSHALL, J. (1883) *Med. Chir. Trans.*, 66, 27.
MOORE, N., and PAGET, S. (1905) The Royal Medical and Chirurgical Society of London Centenary. Centenary, 136.
ROLLESTON, J. D. (1924-25) *Proc. R. Soc. Med.*, 18 (Sect. Hist. Med., 1).
—— (1926-27) *Proc. R. Soc. Med.*, 20 (Child. Sect., 55).
—— (1933-34) *Proc. R. Soc. Med.*, 27, 177.

Carcinoma of Œsophagus: Resection and Œsophago-gastrostomy.—VERNON C. THOMPSON, F.R.C.S.

J. W., aged 53, Labourer.

History.—June 1941: Sudden onset of dysphagia. September 1941: Carcinoma of œsophagus diagnosed by X-ray.

George Street, Hanover Square, in the rooms of the Medical Society of London, and again in the rooms of the Royal Medical and Chirurgical Society at 20, Hanover Square. ·

Cases shown were drawn from all departments of medicine in the widest sense of the word. Dermatology was represented by Radcliffe Crocker, Colcott Fox, Tilbury Fox, Malcolm Morris, and J. J. Pringle; Epidemiology by George Buchanan and Sir Richard Thorne-Thorne; Neurology by Charlton Bastian, C. E. Beevor, Thomas Buzzard, Sir William Gowers and Hughlings Jackson; Ophthalmology by E. Nettleship, George Lawson and Brudenell Carter; Orthopædics by J. Jackson Clarke, T. H. Openshaw and Bernard Roth; Otorhinolaryngology by Sir Felix Semon, Sir Morell Mackenzie and Sir William Dalby; Pædiatrics by Sir Thomas Barlow, J. F. Goodhart and Sir G. F. Still, and Urology by Sir Henry Thompson, Sir George Buckston Browne, W. F. Teevan, Hurry Fenwick and David Newman. As regards my own speciality of acute infectious diseases, the *Transactions* of the Clinical Society show that this subject received much more attention than it subsequently did at the Clinical Section, as is seen from the fact that during the forty years of the Clinical Society's existence there were some fifty cases of acute infectious disease recorded, particularly diphtheria, scarlet fever and typhoid, as compared with only fifteen in the *Transactions* of the Clinical Section between 1907 and 1942.

Undoubtedly the most interesting historical event connected with the Clinical Society was the first medical demonstration held in this country of X-rays nearly fifty years ago. Sir William Hale-White, who was honorary secretary at the time, said: "Early in 1896 the Society invited Professor Sylvanus Thompson, the celebrated physicist, to tell its members about the new discovery. A Special Meeting was held on March 30, 1896, in the Society's rooms in Hanover Square and was attended by nearly 400 members." As the professor did not read a formal paper, the demonstration was not recorded in the *Transactions*, but short notices of the event appeared in the *Lancet* (1896, i, 935) and *British Medical Journal* (1896, i, 875) at the time. Subsequently numerous cases illustrating the diagnostic and therapeutic value of X-rays were reported at the meetings of the Society, and recorded in Volumes 30 to 40 of its *Transactions*. ·

At the time of its amalgamation in the Royal Society of Medicine in 1907 the Clinical Society numbered 572 ordinary members and 16 honorary members, seven of whom were British, viz. Sir William Broadbent, Thomas Bryant, Lord Lister, Sir William Osler, Sir Thomas Smith and Sir Samuel Wilks, and nine foreign, namely John Billings, Wilhelm Erb, Friedrich von Esmarch, William Williams Keen, Theodor Kocher, Ernst von Leyden, Just Lucas-Championnière, Costanzo Mazzoni and Weir Mitchell.

Sir Thomas Watson was the first and most eminent President of the Clinical Society, of whom John Marshall in his Presidential Address before the Royal Medical and Chirurgical Society, of which Watson was a Vice-President, said: "All his titles must yield in significance to that of being termed 'the greatest English Physician of the present century,' a designation which he fairly earned by his professional eminence, his moral worth, his sagacity, his integrity, his undeviating regard for the feelings and interests of his brethren, and by his steady adhesion to those high principles of duty, which he so eloquently expounded in his well-known and often quoted 'Introductory Lecture,' and which made him so fit an adviser on ethical questions relating to our profession." (*See* my paper entitled "Sir Thomas Watson, President, Royal College of Physicians," to appear in a forthcoming number of *The Medical Press and Circular*.)

Of the 19 other Presidents of the Society the most notable were Sir William Broadbent, Sir Douglas Powell and Sir Frederick Taylor among the physicians, and Sir James Paget, Lord Lister, Thomas Bryant, Howard Marsh and Hugh Clutton among the surgeons. The rules of the Society ordained that each President should hold office for two years and that surgeons should alternate with physicians—a rule which was and still is rigidly observed. Each President either in his first or second year of office delivered an Address—a rule which was also faithfully kept by the Society though not subsequently by the Section. Four Presidents indeed, viz. Dr. Greenhow, Sir William Gull, Sir Dyce Duckworth and Sir Prescott Hewitt gave two Addresses, the first being Inaugural and the second Valedictory. The great majority of Presidential Addresses dealt with generalities, and only three had definite titles, viz. those by Sir Prescott Gardner Hewitt on Pyæmia in General Practice (*Trans. clin. Soc. Lond.*, 7, 1874), Joseph Lister, as he was then, on The Catgut Ligature (12, 1881), and H. H. Clutton on *Adolescent or Late Rickets* (39, 1907).

A remarkable custom in the practice of the Society, which, doubtless, owing to life having become much more strenuous, is not now observed by the Section, was the frequent formation of special committees to discuss various subjects or individual cases. Of such committees undoubtedly the three most important were those on myxœdema (21, *Suppl.*), the periods of incubation and contagiousness of certain infectious diseases (25, *Suppl.*) and the antitoxin of diphtheria (31 *End*), of which the members were Dr. W. S. Church, Stephen Mackenzie, Sidney Coupland, Hale-White, Sidney Ringer, William Pasteur (Hon. Sec.), J. W. Washbourn, H. P. Hawkins and last but by no means least, E. W. Goodall (31, 1898). Other interesting subjects discussed by special committees

were The Temperature in Syphilis (3, 1870, 170), Hyperpyrexia in Rheumatism (1882, 15, 261), Excision of Hip-joint (1881, 14, 223) and Joint Disease and Locomotor Ataxia (20, 1887, 271). Reference should also be made to the Supplement (22, 1889) containing additional information concerning the cases reported in the first 21 volumes of the *Transactions* and compiled by a committee of five physicians and five surgeons appointed by the Council at the suggestion of the President, Mr. Christopher Heath.

George Richmond, R.A. pinx.   *S. Cousins, sculp.*

SIR THOMAS WATSON, BART.

The financial position of the Society was eminently satisfactory throughout its course and this is no doubt to be attributed to the business capacity of the treasurers, three of whom—Greenhow, Heath and Ord—held office for ten or eleven successive years. The largest sum expended by the Society at one time was £300 for the publication of the Committee's Report on Myxœdema, £100 of which, however, was defrayed by Dr. W. M. Ord, the Chairman of the Committee.

No account of the activities of the Clinical Society would be complete without allusion to the valuable author and subject indexes of the *Transactions,* occupying two volumes. The first, which was compiled by Dr., afterwards Sir, Archibald E. Garrod, appeared in 1898, and dealt with the thirty years 1868-1897, while the second published in 1919 covered the period 1898-1907.

REFERENCES

BAILEY, J. B. (1895) *Brit. Med. J.* (ii), 102.
BLAND-SUTTON, Sir J. (1930) "The Story of a Surgeon," 59. London.
HALE-WHITE, W. (1930) *Lancet* (ii), 1370.
MARSHALL, J. (1883) *Med. Chir. Trans.,* 66, 27.
MOORE, N., and PAGET, S. (1905) The Royal Medical and Chirurgical Society of London Centenary. Centenary, 136.
ROLLESTON, J. D. (1924-25) *Proc. R. Soc. Med.,* 18 (Sect. Hist. Med., 1).
—— (1926-27) *Proc. R. Soc. Med.,* 20 (Child. Sect., 55).
—— (1933-34) *Proc. R. Soc. Med.,* 27, 177.

Carcinoma of Œsophagus: Resection and Œsophago-gastrostomy.—VERNON C. THOMPSON, F.R.C.S.

J. W., aged 53, Labourer.

History.—June 1941: Sudden onset of dysphagia. September 1941: Carcinoma of œsophagus diagnosed by X-ray.

Operations.—October 7, 1941: Laparotomy and jejunostomy. October 29, 1941: Thoracotomy. Diaphragm incised. Growth involving lower 1½ in. of œsophagus and upper 1½ in. of stomach resected. Stomach closed and cut end of œsophagus implanted into separate incision in stomach. *Biopsy*: Squamous-cell carcinoma. *Convalescence* uneventful. *Present condition.*—Eats normally. Working seventy-two hours a week.

Case of Partial Œsophagectomy for Carcinoma with Extrathoracic Gastro-œsophageal Anastomosis.—HERMON TAYLOR, M.D., M.Ch., F.R.C.S.

Mrs. A. B., aged 60. Used to weigh 11 st. Admitted weighing 6 st. 8 lb. having had six months' history of increasing dysphagia.

Examination.—No notable physical signs except gross wasting. Barium swallow: X-ray showed typical carcinoma 2 in. to 3 in. above cardia.

Operation (8.4.43 after three weeks' preparation in hospital).—No preliminary jejunostomy. Cyclopropane and oxygen anæsthesia by Mr. Stout. Intravenous plasma. Time two and three-quarter hours.

Right thoracotomy removing 7th rib. Operable growth found in the œsophagus behind pericardium apparently extending to 1 in. from the cardia. Œsophagus mobilized from the mediastinum after division of the azygos veins and vascular attachments. The lower 5 in. of œsophagus bearing the growth were resected. Upper end of œsophagus temporarily brought out in the neck between pharynx and right carotid sheath above suprasternal notch. Through an epigastric incision, whole stomach separated from its attachments except the pylorus and the right gastric and gastro-epiploic vessels, completely mobilizing the body and fundus. A pre-sternal subcutaneous tunnel was made between cervical and epigastric incisions along which the œsophagus from above, and the stomach from below, were passed and anastomosed through a transverse opening at the level of the 4th costal cartilage. Ryle's tube inserted for feeding purposes. Wounds closed with immediate expansion of lung.

Post-operative progress.—Oxygen by BLB mask. Sulphathiazole by tube. Cough and sputum on fourth day. The anastomosis leaked on fifth day and caused temporary surgical emphysema followed by infection of the wound and, later, the present fistula. Aspiration of chest on third, fourth, fifth and eighth days produced small amounts of fluid which were sterile on culture. On twenty-fifth day aspiration produced staphylococcal pus (? secondary infection from wound). Rib resection and drainage of empyema. Empyema healed in four months. At the present time the patient is ambulant, is gaining weight and taking food by mouth. The fistula at the gastro-œsophageal junction is a gap 1 in. long and is bridged by an indwelling tube through which the food passes without leakage. The fistula is due for operative closure in the near future.

Comment.—The above operation, which as far as the writer is aware, is a new one, has the following advantages: (1) It provides an œsophageal anastomosis which is unlikely to be fatal if leakage occurs. (2) It restores the continuity of the gastro-intestinal tract after the removal of the growth and it obviates the necessity for further subsidiary operations. (3) The resection and the anastomosis may, if necessary, be performed in two stages. (4) It is applicable to growths anywhere in the œsophagus except the upper end.

Two Cases of Œsophagectomy and Anterior Œsophagoplasty.—R. C. BROCK, M.S.

(1) Mrs. A. B., aged 60, had had difficulty in swallowing for two months. X-ray showed a carcinomatous constriction at the level of the 9th thoracic vertebra confirmed by œsophagoscopy and biopsy. On 25.3.43 the œsophagus was removed by Torek's operation, the organ being divided some 2 in. above the cardia and brought out through a stab wound in the epigastrium as an inferior œsophagostomy.

Convalescence was uneventful after this operation and continuity was restored by a rubber tube through which she ate quite well. On 27.3.43 anterior œsophagoplasty was performed, the skin tube being joined above and below but left open near the lower end to allow exit of a tube passing through into the stomach for feeding. Unfortunately some breaking-down occurred at the junction of the upper end of the tube and the œsophagus and a fistula developed. Attempts are being made to close this by plastic operations. Her general condition continues to be good.

(2) Mr. F. B., aged 60, had had dysphagia for three months and investigation revealed a carcinomatous stricture at the level of the bifurcation of the trachea. On 4.3.43 the œsophagus was resected by Torek's method, the upper and lower stumps of the œsophagus being brought out to the skin surface and the two ends joined immediately by an anterior skin tube. Infection occurred leading to breaking-down of the anastomoses but apart from this the patient made a good recovery and feeding was established by a rubber tube. On 17.6.43 a second attempt was made to perform anterior œsophagoplasty but again this failed. He is now feeding well with a large-bore rubber tube.

Comment.—Both these cases illustrate the difficulties in the way of re-establishing continuity of the œsophagus, though the œsophagectomy itself is well tolerated. A preliminary jejunostomy is definitely desirable.

Transthoracic Resection of Carcinoma of the Cardia with Involvement of the Lower End of the Œsophagus, and Œsophago-gastrostomy.—O. S. TUBBS, F.R.C.S.

J. P., male, aged 56. Admitted for operation 29.4.43.

Complaint.—Epigastric pain and weakness.

Previous history.—Abdominal gunshot wound 1917.

History of present complaint.—In May 1942: Excessive fatigue. August 1942: Severe pain in epigastrium immediately after swallowing food; this lasted for a quarter of an hour and was followed by a dull ache which lasted to the next meal. Appetite good but afraid to eat. No difficulty in swallowing. No vomiting. November 1942: Black stools for three days—felt very weak and was admitted to hospital. Hæmoglobin 34% (Haldane). No abnormal clinical signs apart from secondary anæmia associated with achlorhydria. Barium X-ray examination of stomach revealed no abnormality. Rest, alkalis and iron resulted in almost complete relief of pain and a rise in hæmoglobin to 54%. Discharged after seven weeks. March 1943: Pain more severe than ever before. Vomited a small amount of blood. Readmitted to hospital. X-ray examination again showed no gastric abnormality but gastroscopy (Dr. Charles Fletcher) revealed the borders of a sloughing ulcer near the œsophageal opening.

29.4.43: Transferred for operation. 30.4.43: Transfusion of 2 pints of fresh blood. 3.5.43: Hæmoglobin 72%. 4.5.43: Exploratory laparotomy (Mr. J. P. Hosford). Carcinoma of cardia confirmed. The growth was mobile but involved the abdominal part of the œsophagus, and therefore irremovable by total gastrectomy. Jejunostomy performed. Convalescence complicated by suppurative bronchitis. 27.5.43: Transthoracic resection of growth and œsophago-gastrostomy. Exposure obtained through the left 9th rib bed followed by incision of diaphragm; lower end of œsophagus mobilized and stomach freed by division of greater and lesser omenta; growth resected with proximal half of stomach and 2 in. of œsophagus; stomach closed and œsophagus anastomosed to anterior wall of stomach; diaphragm sutured to partially thoracic stomach; chest closed with intercostal drainage. 1.6.43: Pleural drain removed.

5.6.43: Fluid first given by mouth. 9.6.43: Jejunostomy tube removed. 11.6.43: Allowed up. 24.6.43: Barium X-ray examination of œsophagus and stomach; no stricture at site of anastomosis; barium passed rapidly into stomach.

29.6.43: Discharged. Since discharge, general condition has improved; no pain; no difficulty in swallowing; regurgitates small quantity of watery fluid after meals.

Professor Grey Turner said it was a remarkable occasion and he could not help wondering what the members of the Laryngological Section would have thought when he presented his first completely successful case of œsophagectomy in this very room in 1934, if someone had told them that in less than ten years five successful cases could be shown in one afternoon! The fact that these successful cases could be shown was a complete vindication for what he had urged about the place of operation in the management of malignant disease of the œsophagus. He had always predicted that the day was not far distant when it would be much more generally amenable to surgery. The cases also showed that in the presence of malignant disease the surgeon must never be easily deterred. One of the speakers had mentioned that "pull-through" method which had been employed in the case presented by the speaker in 1934, but he would like it to be clearly understood that he did not advocate that method at the present time. He felt sure that the future of the management of the malignant disease of the œsophagus depended upon the development of the intrathoracic operation but none the less he was not prepared to say that the "pull-through" would never again have a place in surgery. The whole problem was wrapped up in the question of early diagnosis. This ought to be made within a week or two of the presentation of the first suggestive symptoms, if that could be done then probably in many cases the growth would be found limited to the wall of the œsophagus which might still move freely in the bed of cellular tissue in which it lies. This would greatly facilitate the problem of removal. He did not wish to take up the time of the meeting by making detailed remarks about the patients shown but he would like to point out that a very favourable feature was the fact that their average age was just a few months over 57. This was in marked contrast to the majority of the cases with which he had been called upon to deal for most of his patients had been round about 70 and were usually rather worn and often the victims of cardiac and respiratory breakdown. The cases also showed the importance of experience in chest surgery and he was reminded of the remark made in 1918 by George E. Gask, one of the pioneers in thoracic surgery, to the effect that the day would come when the chest cavity might be as freely opened for exploration as the abdomen. But it would be wrong and misleading to give the impression that the problems of œsophagectomy were all solved for there was still a very high mortality which was often disheartening because the cause could not be assigned. Restoration by direct anastomosis after excision of the lower œsophagus seemed on the right lines as exemplified by two of the cases shown, but the speaker knew only too well that there were many difficulties and disappointments connected with the efforts to restore the function of swallowing after excision of the middle portion, and he confessed that he still had considerable doubt in his own mind as to the best method. He was certainly very much impressed with the extrathoracic restoration by using the mobilized stomach as exemplified in one of the patients. One debatable question seemed to be settled by these cases for the five patients showed conclusively that division of the lower part of both vagi had not interfered with restoration to health and activity. These remarkable cases certainly demonstrated the value of the Clinical Section which

was an admirable place to compare results and pool experience for it was in that way that progress lay.

Hæmangiectatic Hepatoma.—KENNETH HERITAGE, F.R.C.S.

Miss M. F., aged 46, was admitted with a three days' history of persistent localized pain in the right iliac fossa. No vomiting. Bowels normal. Micturition normal. Amenorrhœa for the last three years.

T. 98·6°. P. 84. R. 20. No signs of acute appendicitis but a large smooth rounded mass was palpable immediately to the right of the umbilicus. The mass moved with respiration but an interval could be felt between it and the liver and the costal margin. No pulsation could be felt. All pain cleared up with rest in bed.

Urine completely normal on chemical examination, microscopy and culture. Intravenous pyelogram showed normal renal pelves and calices.

Barium follow-through meal showed no abnormality of the stomach or duodenum but the hepatic flexure and proximal part of the transverse colon were displaced downwards by the mass.

Laparotomy (30.4.43) showed the mass to be a pulsatile tumour arising from the undersurface of the right lobe of the liver. The common hepatic artery and its right and left branches were greatly hypertrophied and tortuous and many large vessels could be traced through the liver substance into the tumour. As the intense vascular engorgement suggested that severe hæmorrhage might arise spontaneously or as result of slight trauma it was felt that the tumour should be removed but attempts to separate it from the liver threatened uncontrollable hæmorrhage. Compression of the right hepatic artery arrested all pulsation in the tumour leaving the left lobe of the liver unchanged so this artery was tied in continuity. The tumour shrank, immediately ceased pulsating and was removed without difficulty. The bare area of liver was covered with an omental graft.

The patient made an uneventful recovery.

Dr. F. Parkes Weber thought the tumour might be termed hepatoma only in the sense that its parenchyma consisted of cells resembling hepatic glandular cells. It was separated from the true liver and Dr. Weber suggested that it really represented an attempt at the formation of another liver from a misplaced or separated embryonic rudiment. In such cases the blood supply was likely to be abnormal and in the present case there was a decidedly hæmangiectatic (not hæmangiomatous, he thought) blood supply. He would therefore call the tumour a "hæmangiectatic hepatoma", in the abovementioned special use of the term "hepatoma". namely, as being a tumour or a pseudotumour of E. Albrecht's "choristoma" class. (Compare Dr. Weber's remarks on Dr. E. S. Lee's case, *Proc. R. Soc. Med.*, 1942, 36, 35.)

Psoas Abscess Containing Gas and Fæces, Secondary to a Fistula from the Cæcum.—E. C. B. BUTLER, F.R.C.S.

Mrs. M., admitted 1942. General condition became desperate. Surgical treatment: (1) Ileostomy for eight months. General condition became good. Discharge from fistula less. (2) Right side of colon completely isolated and drained by mucous fistula in transverse colon. (3) Ileostomy closed and ileo-transverse colostomy performed.

Present condition.—Up and walking, general health good. Still some discharge from sinus in thigh and back. Bowels open regularly.

Possible cause of fistula may have been appendix but this has never been proved.

Periarteritis Nodosa with Marked Eosinophilia.—HORACE EVANS, M.D., F.R.C.P. (shown by J. R. TASKER, M.R.C.P.).

Female, aged 47. Admitted to the London Hospital on 15.8.43.

History.—Nine months—muscular pains in legs, tender nodules on the hands and hæmoptysis. Five weeks—sudden loss of vision of left eye.

On examination.—Flushed with fever and tachycardia. Tender nodules on hands, elbows and coccyx. Signs of blockage of left central retinal artery.

Investigations.—Blood-count showed a persistent eosinophilia up to 76% of the total white cell count which was itself increased. Urine contained red blood cells. Biopsy of nodules suggested granulomatous rheumatic nodules.

Dr. F. Parkes Weber agreed that the case was undoubtedly a genuine example of periarteritis nodosa, of a somewhat chronic type, in which the reaction on the part of the tissues to some extent compensated the damage caused by the direct action of the agent—which he thought must be some kind of infective agent. The inflammatory fibroid tissue reaction in this case had apparently prevented the formation of aneurysmal dilatations. though it had caused occlusive lesions. The action and reaction in the lesions had probably (between them) caused the entry of some substance into the circulating blood. which in its turn had excited the excessive eosinophilic reaction. The tender nodules on the hands, he thought, neither macroscopically nor microscopically resembled any kind of rheumatic or rheumatoid nodules and were (in some way) probably a specific expression of the disease process.

Section of Neurology

President—Brigadier HUGH CAIRNS

[*October* 21, 1943]

The Present Position with Regard to the Epidemiology of Poliomyelitis

By Professor S. P. BEDSON, M.D., F.R.S.

A FEW years ago not many of us had any doubts as to the way in which poliomyelitis was spread. It was accepted that this was one of those diseases which was passed from man to man by means of infective droplets; the primary focus of infection was thought to be in the nasopharynx, the virus passing from this situation to the anterior horn cells of the cord by axonal routes. The basis of this conception was a number of well-established observations concerning both the virus and the naturally occurring and experimentally produced disease. It was known that poliomyelitis virus was a highly specialized neurotrope, incapable apparently of developing in any but nerve cells. In the disease as it occurs in man, the virus had been found in the nasopharynx, in the central nervous system and in the stools but only exceptionally in other situations (mesenteric glands) and in the experimental production of this disease in the monkey, of the less artificial methods of inoculation, application of the virus to the nasopharynx had proved the most successful. By a combination of histological study and examination of the central nervous system for the presence of virus at different levels and at varying intervals of time after inoculation both by the intranasal and intracerebral routes, it had been deduced that the virus reached the nerve cells of the anterior horns by axonal routes; in particular histological changes in the olfactory bulbs were found to develop regularly in monkeys infected by the nasal route. Furthermore, the monkey was shown to be insusceptible to infection by the nasal route if, before inoculation, all connexion between the olfactory bulbs and the olfactory mucosa had been severed or the olfactory mucosa had been "tanned" with alum, zinc sulphate or picric acid. No one to-day contests the accuracy of these observations, and it must be admitted that the conclusions drawn from them were by no means unreasonable or illogical. Even the occasional indirect spread of poliomyelitis by milk, for which there is some evidence, was not out of keeping with the view that this disease was spread primarily by infective droplets, since in a condition like scarlet fever, which is spread mainly by infective droplets, milk-borne outbreaks occur. There was, however, one feature of the epidemiology of poliomyelitis which did not fit in with the generally accepted view and that was the seasonal incidence of the disease. Poliomyelitis has its major incidence in the late summer and early autumn unlike droplet-spread infections which are diseases of winter and early spring; at any rate it is at those times of the year that they are most prevalent. This fact led some to question the conception of the droplet spread of poliomyelitis. Toomey, in America, in particular, expressed disbelief and advanced the view that the portal of entry was the alimentary tract. In support of this hypothesis he produced experimental evidence showing that in the monkey infection could be produced by introducing poliomyelitis virus into isolated loops of small intestine or by injecting it into the intestinal submucosa. Whilst not denying that this could be done, Toomey's critics held that the methods used in these experiments were too artificial to have any bearing on the naturally occurring disease and the majority retained their belief in the droplet spread of poliomyelitis.

Work done during the last few years has shaken this belief and gone a long way to substantiate the views of those who, like Toomey, believe that infection enters by the alimentary tract. For instance, where the olfactory bulbs have been examined in fatal human cases there has been a remarkable absence of any histological change. It has been suggested that this might merely mean that in man the transit of the virus

through these structures was more or less unopposed and in consequence left little in the way of structural change, but in the light of the failure of chemical sprays in the prophylaxis of human poliomyelitis, it would appear more reasonable to assume that in man the virus rarely used this route in its transit to the central nervous system.

In the Toronto epidemic of 1937 a 1% zinc sulphate spray was given a thorough trial and found to have no preventive value (Pentecost, 1937; Tisdall *et al.*, 1937). These observations pointing to the relative unimportance of the olfactory mucosa as the portal of entry in human infections acquire even greater significance when viewed in the light of recent work on the presence of the virus of poliomyelitis in the stools of human cases and contacts. It has been known for some time that poliomyelitis virus could be demonstrated in the fæces, but with the exception of Kling, Wernstedt and Pettersson (1911-12) who isolated the virus from this material with some regularity, the majority of workers obtained either negative or inconstant results. The recent studies of Paul and Trask and their colleagues in America have shown, however, that, given an adequate technique, the virus of poliomyelitis can be demonstrated in the stools of human cases with remarkable regularity (Trask, Vignec and Paul, 1938; Trask, Paul and Vignec, 1940; Melnick, 1943). What is more they have succeeded in isolating the virus from the sewage of urban communities in which poliomyelitis was epidemic (Paul, Trask and Gard, 1940). In this investigation 5 out of 19 specimens collected from sewers in the vicinity of isolation hospitals in which cases of poliomyelitis were being nursed yielded positive results. Sewage samples collected at a distance from the hospitals were negative, as were samples collected after the epidemic had ceased. It is interesting to note that whereas positive results were obtained if the specimen of sewage was examined within twenty-four hours of its collection, negative results were the rule with sewage which had stood for thirty or more days, suggesting that the virus is destroyed in sewage fairly rapidly. The work of this group of American investigators has established, however, that the virus of poliomyelitis is excreted in the stools with considerable regularity and that it can be recovered from sewage. Confirmation of this important observation has not been lacking. Piszczek, Shaughnessy, Zichis and Levinson (1941) isolated poliomyelitis virus from the stools in 3 out of 4 cases and from 6 out of 34 contacts in an outbreak involving two schools in a suburban community, whilst negative results were obtained with the stools from 14 non-contacts.

The investigation of an outbreak of poliomyelitis in a family following tonsillectomy reported by Francis, Krill, Toomey and Mack (1942) is even more interesting. This family consisted of the parents and 6 children. On August 22, 1942, 5 of the 6 children had their tonsils removed and by September 5 all 5 were acutely ill with poliomyelitis of the bulbar type; 3 of them died. Poliomyelitis virus was isolated from the stools of all 6 children. The stools from 43 contacts of these 5 cases were examined. Of these contacts 9 were adults; none had positive stools. The child contacts fell into two groups, one, comprising 6 individuals, where the contact was intimate and the other, 28 children, in whom the contact was less intimate. All the children in the first group and 4 in the second group had virus in their stools. There is, therefore, no lack of evidence of this mode of excretion of the virus in human poliomyelitis and this together with the recent demonstration that flies may carry the infection (Paul, Trask, Bishop, Melnick and Casey, 1941; Sabin and Ward, 1941), and the other evidence I have mentioned—the failure of chemical sprays in the prophylaxis of poliomyelitis and the rarity of histological change in the olfactory bulbs in fatal human cases of this disease—suggest most strongly that the common route of infection in man is the alimentary and not the upper respiratory tract. The evidence does not entitle one to say that this disease is never spread by infective droplets; it may well be so spread but if this does occur it would seem to be uncommon. And the acceptance of the alimentary tract as the common route of infection does not imply that invasion necessarily takes place from the intestinal tract, though the frequency with which the lumbar enlargement of the cord is involved would point to the importance of this particular route. In this respect the findings of Faber and Silverberg (1942) in one of their experimental monkeys are of interest. This animal had received virus in fat-coated capsules, had its tongue gently swabbed with virus and had received a high enema of virus all without effect. It finally developed poliomyelitis after having virus sprayed on to the throat, the olfactory mucosa having previously been blocked by spraying with zinc sulphate. The histological evidence suggested that in this monkey, virus had reached the bulb by the intermediary of the 9th and 10th nerves. In all probability, therefore, virus entering by the alimentary tract can pass to the central nervous system by a variety of routes at different levels and this would help to explain the distribution of the lesions in human cases.

It seems permissible, therefore, to conclude that, although in poliomyelitis the virus

may invade the central nervous system from a variety of peripheral starting points, the nasopharynx, the throat (tonsil) or the intestinal tract, it is the last two which are the most important. This would imply that, contrary to our previous beliefs, poliomyelitis is acquired mainly if not entirely by the alimentary route, the virus reaching man indirectly through the agency of contaminated food, milk and possibly water. Whether infection is spread by droplets as well and if so, what is the relative importance of the two modes of spread will be for future investigation to disclose. In any case the recognition of the importance of the alimentary tract as a portal of entry of infection necessitates a recasting of our views of the epidemiology of poliomyelitis and of the measures we may take for its control.

REFERENCES

FABER, H. K., and SILVERBERG, R. J. (1942) *Science*, 96, 473.
FRANCIS, T., Jr., KRILL, C. E., TOOMEY, J. A., and MACK, W. N. (1942) *J. Amer. med. Ass.*, 119, 1392.
KLING, C., WERNSTEDT, W., and PETTERSSON, A. (1911-12) *Z. ImmunForsch.*, 12, 316 and 657
MELNICK, J.,L. (1943) *J. exp. Med.*, 77, 195.
PAUL, J. R., TRASK, J. D., and GARD, S. (1940) *J. exp. Med.*, 71, 765.
——, ——, BISHOP, M. B., MELNICK, J. L., and CASEY, A. E. (1941) *Science*, 94, 395.
PENTECOST, R. S. (1937) *Canad. publ. Hlth. J.*, 28, 493.
PISZCZEK, E. A., SHAUGHNESSY, H. J., ZICHIS, J., and LEVINSON, S. O. (1941) *J. Amer. med. Ass.*, 117, 1962.
SABIN, A. B., and WARD, R. (1941) *Science*, 94, 590.
TISDALL, F. F., BROWN, A., DEFRIES, R. D., ROSS, M. A., SELLERS, A. H. (1937) *Canad. publ. Hlth. J.* 28, 523.
TRASK, J. D., VIGNEC, A. J., and PAUL, J. R. (1938) *J. Amer. med. Ass.*, 111, 6.
——, PAUL, J. R., and VIGNEC, A. J. (1940) *J. exp. Med.*, 71, 751.

Sir Arthur MacNalty : In the epidemiological work at the central Health Department the droplet theory of infection had been regarded as the main explanation for the spread of poliomyelitis, although an intestinal route was not excluded. It had been known for many years that the virus of the disease might be present in the stools of patients, while the abortive forms and the initial stage of the malady were frequently characterized by gastro-intestinal symptoms. In addition, widespread visceral lesions might be found such as hyperplasia of the tonsils, the spleen and lymphatic glands, together with cloudy swelling of the kidney and liver. Certain of the investigators in the New York epidemic of 1916 found some grounds for the belief that poliomyelitis followed the course of a river. This could now be correlated with the presence of the virus in sewage. He noted that Professor Bedson did not entirely exclude the naso-pharyngeal route of infection.

With regard to the incubation period, in experimental observations by Flexner and others this is stated to vary from three to forty-six days, the general period being about eleven days. Clinical observations suggest an incubation period of from two to ten days, and although shorter and much longer periods have been recorded, the average period may be regarded as from three to four days.

Professor Seddon[1] had mentioned certain cases with facial paralysis in the Malta Outbreak. He would like to know if there were many instances of the polio-encephalitic form in this epidemic? Wickman, in the Swedish epidemic in 1905, in over 1,000 cases did not see a single instance. Nor was any example reported in the New York epidemic of 1907 in which over 2,000 cases were observed. This cerebral type of poliomyelitis had been seen not infrequently in England and Wales in recent years. He found this to be a striking feature of the Broadstairs epidemic in 1926 where, out of 55 cases, no fewer than 32 were examples of polio-encephalitis.

Dr. Robert Cruickshank : I think that the possibility of flies acting as vectors of the *virus should be considered. American work has lately shown that the virus can be* recovered from blowflies and green bottle-flies (but not from biting flies) with access to the fæces of acute and convalescent cases of poliomyelitis. I should like to ask Professor Seddon if flies were unduly prevalent at the time of the epidemic in Malta, described by him? Another interesting point was the large number of affected infants in this epidemic; the probability that some of these infants were wholly breastfed would suggest that droplet infection was a factor in the spread of poliomyelitis.

Dr. F. E. Camps : During the last large epidemic of poliomyelitis in this country which occurred in Essex in 1938 it was possible to trace contact cases which I feel might aid the recognition of the incubation period and which possibly throws some light on the mode of spread. The first cases were known to have occurred at Halstead on and after July 1, 1938. On July 15, 1938, four boys at Felstead school contracted the disease, the mode of infection at the time was obscure particularly as the general trend

---

[1] Professor Seddon's paper on Poliomyelitis in Malta, and another by Army Medical Officers in Malta, will appear later in other medical journals.

of opinion was that the disease was spread by droplets. However Dr. Barber, the medical officer of the school, did suggest that it might have been conveyed from Halstead to the school by strawberries which were eaten on the prizegiving day some time before. Now in light of more recent knowledge this theory does appear to be a possible explanation. All four boys who contracted the disease were in the same house and their beds were made by two maids who went to and fro between their own homes and the school; it is therefore of considerable interest that on August 5, 6, 7 and 8, 1938, three brothers and sisters of one of the maids developed the disease and that in a neighbouring cottage a small child who was on a visit from Southend from July 15, 1938, to August 2, 1938, later developed poliomyelitis at Westcliff on August 12, 1938, and two other children in another cottage fell ill on September 1, 1938, and September 18, 1938. His two cousins had visited him at his home after he had returned on August 4, 5 and 6, 1938, and they in their turn contracted the disease at Yarmouth whilst on holiday on August 18 and 21, 1938. Similarly the brother of the other maid developed the disease on August 12, 1938.

It seemed that a fæcal-contaminated milk or water-borne spread would not explain all cases in the same way as the droplet theory would have done had the season been epidemiologically incorrect, but the possibility of some combination of the two, such as hand to hand fæcal or droplet contamination might be a possible explanation which would fit in with all the known facts.

A further observation made during the epidemic was that cases which were diagnosed early in the disease and rested at once tended either to have no paralysis or if paralysis did occur to get complete recovery. Also those persons who were known to have taken violent exercise appeared to become paralysed in the muscles which were most used and a possible explanation would seem to be an exhaustion of the anterior horn cells rendering them more susceptible to attack by the virus.

Professor Seddon in reply to Sir Arthur MacNalty's question: Apart from the fourteen cases of respiratory paralysis, all fatal, the only cases of brain-stem involvement were as follows: (a) One case of polio-encephalitis; (b) the forty cases of facial paralysis; in two of them the 6th cranial nerve was involved; (c) one case of involvement of the 6th nerve, with paresis of the lower limbs.

In reply to Dr. Robert Cruickshank's question: Flies were unduly prevalent in Malta before and at the time of the epidemic. In the devastated areas there were quantities of garbage that could not be cleared away, as well as the sewage that was used for fertilizing crops. The factor of breast feeding in relation to droplet infection may be of importance; but the contact between a breast-fed child and its mother would hardly be so intimate as the contact between the child and those with whom it slept. Only 98 of the 396 children had a bed or cot to themselves, and in no single case was the affected child in a room by itself at night.

Section of Anæsthetics

President—R. J. MINNITT, M.D., D.A.

[*October* 1, 1943]

The History and Progress of Gas and Air Analgesia for Midwifery

PRESIDENT'S ADDRESS

By R. J. MINNITT, M.D., D.A.

ABOUT the year 1932 many public bodies were awakening to the urgent need that something should be done for the relief of pain during childbirth, and in response to a request from the Clinical Investigation Sub-Committee of the Medical Board of the Liverpool Maternity Hospital to suggest any proposals that could be considered on the subject, I replied that some form of oral administration for assuaging labour pains had yet to be found, and that I would like to be associated with the research work.

The fact that I had often noticed that although a patient undergoing teeth extraction with gas struggled violently, yet later had no recollection of the actual operation, encouraged the intention to try out the drug in midwifery, and early in 1933 I remember the late Dr. Howard Jones saying that he thought it could be administered on the injector principle. This stimulated me to consider the working out of details and make the experiment, but my view was that it should be a mixture of nitrous oxide and air, and not pure gas. Gas and air was first used in America, and was administered with a machine invented by Dr. McKesson, the proportion of gas being 70%. The unsatisfactory results were due to a too high percentage of gas, and I felt that if the proper proportions could be found a safe and reliable analgesia would be produced.

Dr. A. A. Gemmell wrote on July 4, 1933, to ask me to suggest a possible scheme for research on anæsthetics in labour at the Liverpool Maternity Hospital, the aim being to discover a means of alleviating the pains of labour without interfering with the uterine action. Further, the method was to be one applicable to general practice, and one which the doctor could safely leave in the hands of the midwife to carry out in his absence.

On July 19, 1933, Mr. A. Charles King and I considered the adaptation of a McKesson oxygen therapy apparatus for the purpose, and during the next two months I collaborated with him in the construction of an intermittent flow apparatus for administering gas and air inhalations.

About the middle of September the machine (fig. 1) arrived, together with a Devonshire cylinder stand, and a month later I instructed Dr. Hilda Garry how to use it for the first case at the Liverpool Maternity Hospital, and evolved the technique of administration. Four days later it was shown in London at the General Meeting of the Association of Anæsthetists of Great Britain and Ireland. It had then been employed in four cases.

Shortly afterwards Dr. John Elam introduced the machine at the Wellhouse Hospital, Barnet, and from this time investigations were being carried out with the apparatus at these two places under my direction and control. Details of 121 cases were recorded at the Liverpool Maternity Hospital, and of 58 cases conducted at the Wellhouse Hospital, Barnet. These analyses and reports were incorporated in the paper which I read at the Liverpool Medical Institution in February 1934, entitled "Self-administered Analgesia for the Midwifery of General Practice".

A month later Professor A. Leyland Robinson wrote to the Council of the British (now Royal) College of Obstetricians and Gynæcologists, saying that the apparatus for administration of gas and air had given extraordinary results in hospital, and had already proved itself to be of excellent value. He suggested that the method should be given a trial in domiciliary practice. Some research having been undertaken at the Liverpool Maternity Hospital it was established by electro-cardiographic examinations of women to whom gas-air analgesia was administered that these were not influenced to any extent by the patients' experiences. It was also found that the second stage of labour was not prolonged. I read a paper at a Meeting of this Section on May 4, 1934 (*Proceedings,* 27, 1313) upon the subject, and a ciné film, kindly made for me by Mr. C. Macintosh Marshall, was shown of actual administration to patients. I also demonstrated the apparatus at University College Hospital and Queen Charlotte's Hospital, and described the technique at the Royal Free Hospital. Other London hospitals quickly acquired the apparatus, and machines were installed at the Royal Infirmary and at the Walton Hospital, Liverpool, and St. Mary's Hospital, Manchester, soon afterwards.

Dr. Hilda Garry, who had been appointed by the National Birthday Trust Fund, supervised (under my direction) all the administrations in the Liverpool hospitals, and the following analysis of 1,025 cases conducted during 1933, 1934 and 1935, gives some indication of the value of the method:

(1) Relief from pain was good in 952 (92·8%).

(2) Length of time gas and air was administered:

Over 4 hours	80
Between 2 and 4 hours	169
Between 1 and 2 hours	239
Under 1 hour	464

(The stage in labour already reached on admission to hospital accounts for the largest number being under one hour.)

(3) Number of forceps deliveries in the series, 56 (5·5%).

(4) Number of stillbirths in the series, 19 (1·8%). (One unexplained, the remainder due to obstetrical causes.)

Within nine months of its inception gas and air analgesia in midwifery went through a very difficult period. In many places midwives had been using the method under the direction of a medical man, but not under his personal supervision. In consequence, objections were raised in certain quarters, which resulted in action being taken by the Central Midwives Board to insist upon personal medical supervision, and so the development of the procedure was arrested. In July 1934 the matter was taken up by influential people, including Mrs. Stanley Baldwin (now Lady Baldwin). Deputy Chairman of the National Birthday Trust Fund, the late Lord Knutsford, and others. It was left in abeyance, however, in view of an investigation which was about to be carried out into the use of analgesics in labour by the British College of Obstetricians and Gynæcologists, at the request of the National Birthday Trust Fund, who generously defrayed the cost. Dr. Z. Mennell was nominated by the Association of Anæsthetists to give advice as to the actual analgesics employed. Thirty-six hospitals throughout England, Wales, Scotland, Northern Ireland and the Irish Free State, participated, and the findings were anxiously awaited. A report was published in January 1936 with conclusions and recommendations. This prepared the way for the publication of regulations issued by the Central Midwives Board, governing the administration of gas and air by a midwife with a recognized apparatus.

An Advisory Committee on the administration of gas and air by midwives, under the Chairmanship of Sir Comyns Berkeley, was set up by the Central Midwives Board in January 1937. Various meetings were held to discuss the definition of an approved apparatus for the administration of gas and air; and a desirable curriculum for a course of instruction to midwives, and to frame recommendations for the approval of institutions for the purpose of conducting such courses of instruction. Two months later the Government Chemist made a report on the proportions of nitrous oxide in the gas-air mixture delivered under normal inspiration by apparatus submitted by the Committee for testing. This was found to be not more than 45% nitrous oxide in air. It was decided, therefore, that the specification of an approved machine should include that of the delivery of not less than 55% air as an essential condition, together with other definitions.

Hospitals which carried out the original investigation were authorized to give instruction in obstetric analgesia, and grant a certificate. Other hospitals which desired to do likewise could be approved by the Central Midwives Board under certain conditions.

I have been informed, through the courtesy of Mr. L. Farrer Brown, Secretary of the Central Midwives Board, that up to date 1,784 midwives, and 485 pupil midwives, have been found proficient in the use of a recognized apparatus, although the list is not yet complete, since the Board is at present engaged in compiling a register. I am gratified to know that these numbers include 353 candidates in twenty groups, who have received instruction and gained the certificate at the Liverpool Maternity Hospital since January 29, 1937.

The course of lectures I deliver at this hospital in obstetric analgesia (which are four in number) cover the history of drugs, description and demonstration of apparatus, the theory and practice of administration of gas and air analgesia, and the rules and regulations for its use by midwives. At the end of the course each candidate for the certificate is examined for about ten minutes by both myself, as the Honorary Anæsthetist, and a member of the Medical Board, the Sister Tutor or Labour Ward Sister being present. A certificate is granted if practical knowledge of the subject is shown.

In 1936 Mr. L. Carnac Rivett made suggestions for the design of the Queen Charlotte model, which was very convenient to carry. One of its features was an irremovable cylinder key incorporated in the case. Other machines produced during 1936 and 1937 were built on the lines of the well-known Walton gas and oxygen dental apparatus, and by invitation I showed one of these—the midwives' model—at the British Medical

Association Meeting held in Oxford in July 1936. The latest machine which is now in course of manufacture is the incorporation of its principal working parts in the compact Queen Charlotte case (fig. 2).
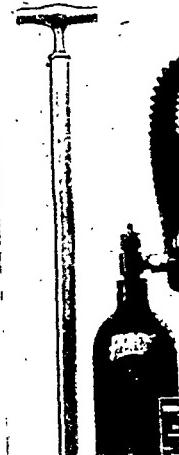
FIG. 1.
The first Minnitt Gas-Air Analgesia Apparatus
used October 16, 1933.
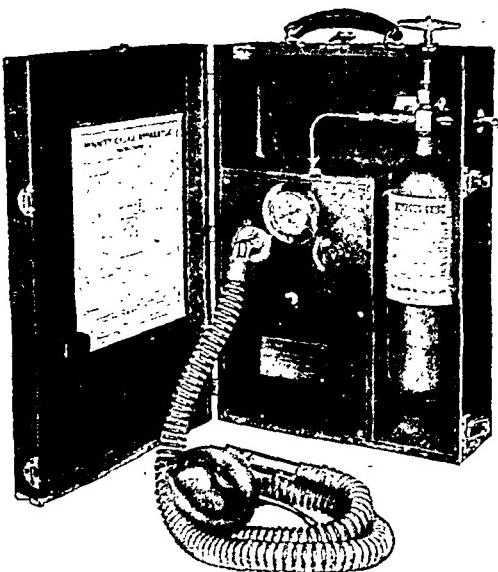
FIG. 2.
Minnitt Gas-Air Analgesia Apparatus (latest model).

I am not going to describe any mechanical details, but wish to draw attention to certain factors that have been found of importance for obtaining satisfactory results in administration. Two points should receive especial emphasis:

(1) *Ante-natal tuition* of the patient is very essential, in order that she should be thoroughly conversant in the use of the machine before labour commences. This gives her confidence and familiarizes her with what she has to do. The time is ideal for training, as there is no distraction by pain and distress. I think the value of this cannot be over-estimated.

(2) *The timing of inhalation.*—At a meeting of the Section of Obstetrics and Gynæcology held on February 19, 1937, I was present at the demonstration given by Professor Chassar Moir of a new type of apparatus for the self-administration of nitrous-oxide gas during labour. The chief feature in technique was the inhalation of two deep breaths of pure gas before the onset of each pain. Correspondence took place between us in the *British Journal of Anæsthesia* of April and October 1937 and January 1938 with reference to the relative merits of the two procedures—pure gas *versus* gas and air.

I conducted some experiments on myself with the help of Dr. R. Penn Harbord, Demonstrator in Anæsthesia, University of Liverpool, who also confirmed my observations. We found that two or three breaths of pure gas produced the first signs of analgesia in sixteen seconds. This was five to eight seconds quicker than with the standard gas and air machine. In thirty seconds the analgesic effect was the most intense; it then declined gradually for fifteen seconds, and became practically absent in sixty seconds. At thirty seconds the gas and air machine produced a state of analgesia as intense as the pure gas machine, but this was maintained as long as inhalation continued.

When using the pure gas method for patients in labour there was a variable amount of relief for the pains when they were not long in duration or severe in character, and this was more rapidly obtained than with gas and air, but in many cases the analgesic effect had worn off before the pain was over, and the patient complained in consequence. In a number of cases there was some cyanosis after the inhalation, which soon disappeared.

It may be of interest to note that a special attachment embodying Professor Chassar Moir's suggestion of enabling pure gas to be inhaled from a bag until exhausted (which amounts to two or three deep breaths) can be fitted to a gas and air apparatus, and then, as proposed by Dr. Elam, inhalation to be continued with gas and air of the standard percentages.

The advantage of speed claimed for the pure gas method, however, can be compensated for by making certain that gas and air is inhaled in the first stage of labour in sufficient time before the onset of a pain to ensure adequate saturation of the blood, and in the second stage in the interval between the pains, so that expulsive efforts can be made by the patient.

The periods of rest obtained between the pains due to the effect of nitrous oxide and air intermittently administered have a most beneficial influence in conserving strength, and in producing a sense of well-being which is of such value in the convalescence. Amnesia of the delivery is also a conspicuous feature.

As so much success had been attained in the relief of the pains of labour it was thought that the method could be applied for diminishing painful sensations in other conditions.

In the David Lewis Northern Hospital, Liverpool, the gas and air apparatus has been employed in the necessary dressings associated with surgery, and on many occasions it has been found a great boon. Such types of painful dressings include—perineal after excision of the rectum, deep sinus after nephrolithotomy, those following operation for
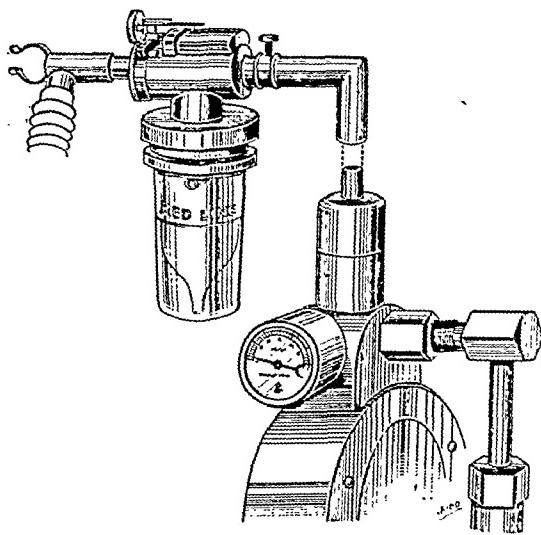
FIG. 3.

Calibrated vaporiser with adapter for attachment to original Minnitt Gas-Air Apparatus.

mastoid, deep anal fistulæ, osteomyelitis of the leg, rectal dilatation, and removal of radium needles from the breast.

This means of relieving pain should be at the disposal of every hospital out-patient department.

In order to enhance the value of analgesia, and for acquiring a transitory anæsthesia in suitable cases, other anæsthetic drugs can be combined with gas and air by fitting a Rowbotham's bottle, or its equivalent, on to the original apparatus by an adapter (fig. 3). Trichlorethylene (trilene) is admirable for this purpose, although great care must be exercised in its use. In one case I have seen tachypnœa, as described by Langton Hewer.

Here are three constructive suggestions for the future:

(1) Midwives and pupil midwives should have the best training that can be given, and consequently those lecturers who are in the position to assist with this tuition should themselves be well acquainted with the details of the technique they have to teach. The provision of special opportunities for discussion concerning instruction in obstetric analgesia might be of much help.

(2) In order to make apparatus available for the largest possible number of patients, depots should be provided where midwives could obtain machines ready for use in their districts. This should not be an insuperable problem when the war is over.

(3) One of the greatest obstacles with which the midwife has to contend is the regulation about the extra person being present at the time of the administration. As I have already mentioned this has been somewhat relaxed, but not enough. I look forward to the day when the rule can be so modified as to remove the difficulty that is now experienced, and enable the patient to be provided with the necessary relief, without at the same time losing anything that is requisite for safety.

Section of Radiology

President—N. S. FINZI, M.B.

[*October* 15, 1943]

Impending New Developments in Radiotherapy [*Abstract*]

PRESIDENT'S ADDRESS

By N. S. FINZI, M.B.

IN the past improvement has occurred along two lines of radiotherapy: (1) More accurate measurement of the dose at the lesion, and (2) decrease in wave-length of X-rays, from an increase in the exciting voltage. Researches into the first-named are steadily proceeding. As to the second, our million-volt apparatus at St. Bartholomew's Hospital, secured through the generosity of Mrs. Meyer Sassoon, has demonstrated that results have been obtained in some forms of malignant disease which were previously impossible and that in some other forms, but not all, there is improvement over the lower voltages.

The inventon of the cyclotron by E. D. Lawrence, the canalization of the beam by Hopwood and Chalmers, and the work of Aebersold had already resulted in Dr. J. H. Lawrence having been able to start work on neutrons for medical and biological purposes in 1938, but there was only one cyclotron available and it was of rather low power, 8 million electron volts (M.e.v.). There were so many physical questions requiring solution too that there was little time for the use of the cyclotron by medical men and no possibility for continuous research. Also there were frequent breakdowns in the cyclotron itself. In 1939 a new cyclotron to be used for medical and biological purposes was finished. The maximum energy of the neutrons from this was 21 M.e.v. A giant cyclotron to deliver energies of 100 M.e.v. was under construction and was due to have been completed this year, but that will probably be mainly for physical work. It is in fact in use at the present time. Since September 1938 Drs. Robert S. Stone and John C. Larken have been working with this 21 M.e.v. cyclotron measuring quantity by a special unit which they call a neutron roentgen (N) and which is probably equal in biological effect to 6 r of X-rays, as judged by the threshold skin reaction. They come to the conclusion, working only on advanced cases, that the effect of neutrons is such as to encourage further study in selected cases. These results will, of course, have to be confirmed and much more work requires to be done, and is being done, on these and other lines.

In artificial radio-activity, the use of labelled atoms, which can be detected and measured by their radio-activity was obviously going to be of great importance to physiologists and others. The employment of this in plant physiology is demonstrated by this autogram of radio-active phosphorus on a tomato plant. It is seen that the radio-phosphorus is deposited in the pulp and to a much greater extent in the unripe seeds: the ripe seeds, however, contain none. Radioactive hydrogen in a drop of water dropped on a leaf can be traced into the vascular system of a plant, showing both the fact and the path of its absorption.

Obviously there are very many problems awaiting solution by this means in plant physiology and pathology but they are at least equalled by those capable of solution in animal and human physiology and pathology. Some of this work has already been started in the U.S.A., but probably the war has interfered with it.

Induced radio-activity also has a use in radiotherapy. If a certain radio-activated atom were deposited in some particular tissue there was the possibility of getting a much bigger dose of radiations to this tissue with only a minimal effect on other tissues. Examples of this are being tried, such as the use of radio-active iodine in the treatment of hyperthyroidism and that of radio-active phosphorus in the treatment of leukæmia. In the first case the iodine is deposited in the thyroid selectively and to more than double this amount in

thyrotoxic cases. A heavy homologue of iodine, element 85, is also a possible remedy for hyperthyroidism in view of the firmer combination it forms in the thyroid tissue. The uptake of radio-iodine and element 85 in other tissues was less than 1% of their concentration in the thyroid (Joseph G. Hamilton, *Radiology*, 39, No. 5, 441).

Low-Beer, J. H. Lawrence, and Stone have worked with other radio-active isotopes. It has been found that radio-phosphorus is deposited selectively in bone, bone-marrow, leukæmia tissue, neoplastic tissue and any rapidly growing tissue. Owing to the short life of radio-active phosphorus and radio-active iodine, these substances have not the dangers of the injection of radium and of thorium salts. In view of the distribution of the activated phosphorus it was evident that it must be tried in leukæmia and some of the other reticulo-endothelial diseases. While it is too soon to assess their value relatively to X-ray and radium treatments, the authors say: "In the treatment of chronic myelogenous leukæmia, chronic lymphatic leukæmia, and lymphosarcoma, some remarkable responses have been obtained and some unsatisfactory ones with widely varying methods of dosage." Good results have also been obtained in this group with polycythæmia vera. In any new treatment the question of dosage is always a difficult problem: big or small doses, frequency and interval of administration and duration of treatment. It will be a long time before these factors can be worked out.

Radio-active strontium is selectively deposited in bone and its value in the treatment of neoplastic diseases of bone is being investigated; activated calcium is unsuitable, because of the small amount formed and its short life.

Activated chromic phosphate is also being investigated in the treatment of neoplastic diseases.

There must be a vast field for the use of these and other artificially radio-activated substances. It is quite possible that they may become available for other purposes, such as the local application of a very short-lived radiation by injection into the tissues or even by external application of radiations of different wave-lengths.

An X-ray apparatus of the compressed-air-insulated electrostatic type is already in use in the United States generating 3,000 kV. and the physical characteristics at this voltage have been worked out (Trump and Cloud, *Amer. J. Roent.*, 49, No. 4). The clinical stage is, of course, only in its infancy, and it is to be hoped that it will be worked out with the same care with which Mr. Ralph Phillips has worked out the clinical results of our million-volt apparatus at St. Bartholomew's Hospital.

The next invention that has emerged during the war is that of the betatron. A device somewhat similar to the cyclotron has been developed by Dr. Kerst of Illinois University, which will produce very high-speed electrons and thus very short wave-length X-rays. Five million and twenty million volts have already been obtained and a betatron to give one hundred million volts has been constructed. Its radiations are now undergoing investigation. The whole machine is extraordinarily compact in view of its output, and with the improvements resulting from shortened wave-lengths there is no question that these ultra-voltage or mega-voltage X-rays have got to be tried in the human being after suitable experimental work on animals.

Depth doses for 5, 10, 15, and 20 million volts have been worked out by Koch, Kerst and Morrison. The most striking difference is that with increasing voltage the maximum ionization occurs further and further from the surface, so that the point of maximum dose is as much as 3 or 4 cm. deep and this maximum can be several times greater than the surface dose. Thus the limitations imposed by damage to the skin and subcutaneous tissues will be much diminished, although there will probably be other difficulties to take their place. In the case of the 20 M.e.v. betatron the maximum intensity of irradiation is at 3 cm. from the surface and is more than three times the surface dose. No doubt with the 100 M.e.v. betatron we shall obtain some other extraordinary features, in fact we may have to consider the exit port of the rays as more important than the inlet for with the 20 M.e.v. the dose at 10 cm. is still 225% of the surface dose. (Fig. 1.)

At 20 M.e.v., however, we shall get artificial radio-activity which may be either an advantage or a disadvantage; we shall also get some degree of neutron formation. At 100 M.e.v. both will be much more marked. Thus it is evident that the path of the investigators will be beset with unforseeable difficulties which can only be indicated by animal experiment, especially when we realize that all elements can be made radio-active. Most of the elements activated have only very short half-value periods. At their threshold their production is minimal, at higher voltages it increases. These facts may save us.

Both with the cyclotron and the betatron the radio-active elements produced can and will be used at a distance from the machine; sometimes a great advantage. It is of the greatest importance to the patient that the control of these remain in the hands of an expert, who must be a doctor with radiological training.

Problems of protection will undoubtedly arise, but to a certain extent they are assisted

by the rays tending to go in the same direction as the electrons which are flowing out of the betatron and to be a relatively narrow beam in the direction of their projection, also almost all the scatter is forward. It may be possible further to control the beam by controlling the electrons with magnets after their emergence from the betatron and to get the same type of effects which one can with a lens, only converting them into X-rays when one is ready to do so. How much such a suggestion is feasible I do not know.

It is now several years since Spear discovered that by suitably adjusting the time relationship between doses it was possible to get results in cultures with doses that were very much smaller than those ordinarily used to produce the same effect, and ever since then I have urged that the time factor for the treatment of malignant disease should be ascertained to see if we could not here get some results by a special time-distribution of doses.

We should also like to hear something about combined X-ray and stilbœstrol treatment.
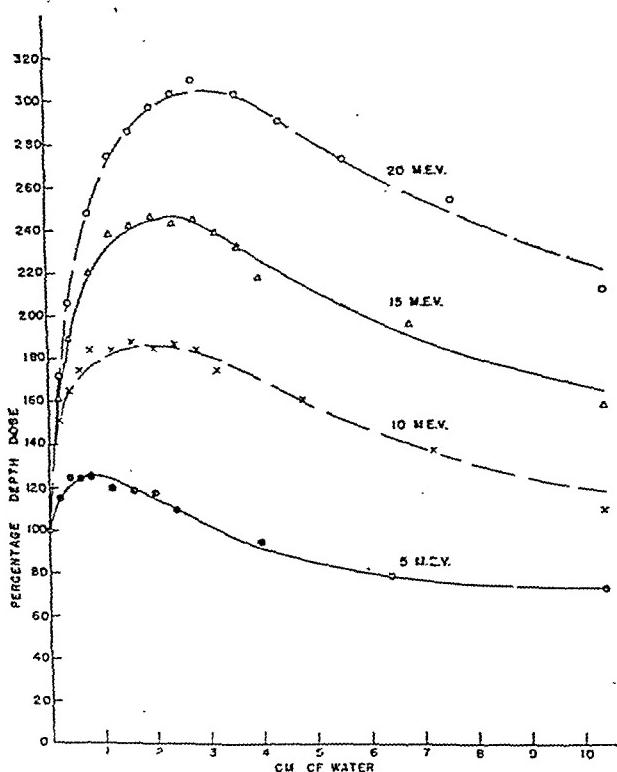
FIG. 1.

Experimental results referred to surface dose. Target-to-surface distance 45 cm.
(From *Radiology*, 1943, fig. 4, 40, 124.)

Dr. Frank Ellis: There is an electrostatic type of generator scheduled to provide 3 million volts in process of erection at present by Grimmet at the Hammersmith Post-Graduate Hospital. There are, I think, two cyclotrons in this country. One at the Cavendish Laboratory and one in the care of Professor Chadwick at Liverpool. The use of the cyclotron opens up certain possibilities of importance. It is most used, of course, for producing artificially radio-active isotopes. It seems possible that radio-active phosphorus, used so far in treating leukæmia in San Francisco and having a relatively long half-value period, about fifteen days, may be of value in treating cancer because the phosphorus may be deposited in the nucleus of cells since nucleoproteins contain phosphorus. If this turned out to be the case, the radiation would be available at the most vulnerable spot of the malignant cells. The more rapid division of the malignant cells suggests that they would take up relatively more of the phosphorus than most normal cells, although rapidly dividing normal cells would also be vulnerable.

The possibility of undesirable genetic effects resulting in gene mutations in the reproductive cells must be borne in mind as a possible effect of therapy by artificially radio-active substances.

A point on which Dr. Finzi did not touch but which seems to be of considerable importance in future development is the possibility of using electrons instead of X-rays from the betatron. Everything depends of course on whether it is possible to get the electrons out of the betatron, though I believe this has been achieved. The intriguing possibility emerges of being able, if a parallel beam of electrons can be obtained, of choosing the voltage of the electrons so that they are absorbed at the requisite depth with little or no absorption elsewhere. The 99·9% waste of electron energy associated with the production of X-rays would in this case be avoided and the dosage of normal tissues might be reduced to a minimum. Careful control of dosage would be necessary but not impossible. Exposures would probably be of the order of seconds or even fractions of a second.

I should like to ask Professor Mayneord if the production of X-rays from electron therapy need be considered seriously. Assuming that an electron dose equivalent to 6,000 r X-rays were used, we should have only about $\frac{1}{1000}$ of this, i.e. 6 röntgens transformed into X-rays. The volume dose from this even if the "target" from which they were produced was tungsten would be very small. As the target is composed mostly of small atomic number elements such as calcium, carbon, oxygen and hydrogen, the "quality" of the X-rays will be such that apart from the high generating voltage they may not be very penetrating. In any case the quantity, as suggested above, would seem likely to be small.

Professor W. V. Mayneord: Dr. Ellis's argument is based on the presumption that the method of loss of energy of an electron is the same at the very high energies under consideration as at relatively low voltages. This however is not in accordance with the modern theory of such very fast electrons. If the energy of the particle is of the order of 100 million electron-volts practically the whole of the loss of energy of the electron will be by radiation even in materials of as small atomic number as air and water. This energy would be expected to be lost in emission of relatively large quanta, of the order of the electron itself. There is to be expected a critical energy (about 10 million volts for lead and 100 million volts for air and water) above which electrons would lose energy almost completely by radiation.

Dr. George G. Binnie: Dr. Finzi has asked for information on the combined X-ray and stilbœstrol treatment of carcinoma of the prostate. I have no experience of this but I have been treating other tumours by the combined method and by stilbœstrol alone, and my present impressions are that some tumours, e.g. certain carcinomas of the breast, will regress with stilbœstrol alone, an exceptional one being apparently cured. Other tumours, e.g. carcinoma of the bladder and lung metastases from carcinoma of the breast, may regress if a combined method of treatment is used. In a third class of tumour, e.g. carcinoma of the rectum and colon, the combined method causes no immediate appreciable change in the size.

My investigations have been repeatedly interrupted by breakdowns in the therapy apparatus owing to difficulties caused by the war, so I have to regard my results as inconclusive. Time may be an important factor, six months or more may be required where the combined method is used.

Dr. Finzi (in reply to Dr. Ellis): Fast electrons have been tried in the past, but so far have met with no success. Their effect is destructive and not selective, so that although an intense local effect is produced it is only that of a cautery. The great advantage of X-rays is that the same dose has a greater effect on the disease than on the normal tissues.

Section of the History of Medicine

President—Sir WALTER LANGDON-BROWN, M.D.

[*October 6, 1943*]

Some Chapters in Cambridge Medical History.—III. William Heberden and the Age of Reason[1]

PRESIDENT'S ADDRESS

By Sir WALTER LANGDON-BROWN, M.D.

IN the retrospect there is a certain feeling of flatness about the eighteenth century: almost the impression of an alluvial valley through which the river of time passed between the torrents of the sixteenth and seventeenth centuries on its way to the turbulence of thought in the nineteenth and the violence of action of the twentieth. But this impression can be exaggerated. After all, the century had enough war even to suit modern demands; we lost the American colonies but founded a new Empire; despite corruption which shocks us to-day our political system took firmer shape, while literature, art and architecture flourished exceedingly. True, poetry declined to a wearisome imitation of the classical and Miltonic diction, which Cowper implicitly, and Wordsworth explicitly set themselves to break up. And herein we may trace a justification to the charge of flatness; the Age of Reason lacked imagination. Mark Rutherford illustrated this by saying that the curious dryness of the criticism of Shakespeare then was because there was so much in Shakespeare to which the eighteenth century could not respond. The Universities played no conspicuous part in the intellectual life of the country; this I should attribute largely to the fact that with some exceptions Fellows had to be in Orders and the current Natural Theology however edifying was not exciting.

In medicine the gold-headed cane symbolized the rise in social status and wealth of the physicians. Men like Radcliffe and Mead lived in a style unequalled even in the palmy days of Victoria, and one which will seem incredible in the future. Samuel Johnson said of Mead that he "lived more in the broad sunshine of life than almost any man". It did not help medicine at Cambridge that for ninety-three years of the century there were only two occupants of the Regius Chair. Christopher Green appointed in 1700 held office until his death in 1741, at the age of 90, but during the last two years he had a deputy who became his successor. During Green's reign there was the famous controversy between the Royal College of Physicians and the Universities, the former demanding their licence before a medical graduate could practise in or within seven miles of London, and the Universities had to undertake to make their medical degrees strictly conformable with the statutory qualifications. And with good reason, for the results of examinations were biased by favouritism and the granting of degrees by royal mandate was rife. Neither Green nor his successor Russell Plumptre, who held office for fifty-three years, seem to have published anything or to have held much of a position in the medical world. Plumptre appears to have served one year on the staff of Addenbrooke's Hospital but no more. The mistake of his appointment to the Chair was all the more glaring as the brilliant William Heberden was available. Yet Plumptre came of a family that provided able men and women for two hundred and sixty years, from Huntingdon Plumptre of Nottingham to Dean Plumptre of Wells. Russell's father was President of the Royal College of Physicians for six years and his cousin became President of Queens' College. Nevertheless, the industrious annalist of the College of Physicians could find no more to say of him than that he was "for many years father of the University and the longest resident that had then been known". Even that was not true, for his immediate predecessor Christopher Green had lived to be older and was resident longer than Plumptre.

In spite of these drawbacks, there were three events of primary importance to Cambridge medicine during the century, the establishment of certain laboratories, the foundation of Addenbrooke's Hospital and the gallant effort of William Heberden to institute a rational system of materia medica and therapeutics. It will be convenient to deal with each of these events in turn rather than to observe a strictly chronological order.

[1] Chapter I. "John Caius and the Revival of Learning," *Proc. R. Soc. Med.*, 35, 61. Chapter II, "Francis Glisson and the Insurgent Century," *Proc. R. Soc. Med.*, 36, 17.

In the year after Queen Anne had ascended the throne, Richard Bentley, Master of Trinity, established in what is now called the Old Bursary what he described as an "elegant chymical laboratory" for Francis Vigani, who had just been appointed the first University Professor of Chemistry. Vigani who was born in Verona settled in Cambridge in 1683 and gave private tuition in chemistry and pharmacy. The professorship created for him was only titular and in recognition of the fact that he had "taught chemistry with reputation" in Cambridge for twenty years. His drug chest, which is preserved in Queens' College, has been fully described by Mr. Saville Peck before this Section. But this room in Trinity may also be regarded as the first physiological laboratory, for here Stephen Hales, Fellow of Corpus, applied his training in physics under Isaac Newton to physiological problems. He was the first to measure blood-pressure and made many other important observations in animal and plant physiology, besides studying problems of ventilation. Indeed he had been called the Harvey of plant physiology. His incursion into medicine was, however, less successful, as I showed in my paper on David Hartley. In 1716 the professors of anatomy and chemistry were accommodated, if that is the right word for such cramped quarters, in a house close to the old University Press. The professor of chemistry soon migrated to other quarters, but it does not appear likely that the study of chemistry can have been very seriously pursued, for when a vacancy occurred in 1764 Mr. Watson of Trinity was appointed through the influence of the Duke of Newcastle, then Chancellor, although it is recorded that "he knew nothing at all, had never read a syllable on the subject, nor seen a single experiment in it". After holding office for seven years, during which time he does appear to have acquired a real knowledge of the subject, he became Regius Professor of Divinity and finally found his proper vocation as Bishop of Llandaff. Nor can the first professor of anatomy, George Rolfe, appointed in 1707 have been very active, since in 1728 he was deprived of office for neglect of duty. At first dissections seem to have been carried out in the Old Schools, and it is to be feared that the body-snatchers made their contribution, for Laurence Sterne, who died in London from tuberculosis in 1768, appeared a week later on the dissecting table there. A grim return to his old University! Evidently the undergraduates had played a part in such body-snatching earlier, for when Matthias Mawson, Master of Corpus Christi College was Vice-Chancellor from 1730-32 he caused a Grace to be passed in the Senate to prevent this. In the words of Robert Master's History of the College (1753): "The practice of digging up human Bodies in the Church-Yards of the town and the neighbouring villages and the carrying them into Colleges to be dissected which became more common about this time, although to no small offence to all serious people was now provided against, it having been hitherto omitted; and the Disturbances which this scandlous Practice caused between the Scholars and Inhabitants prevented." The way of the anatomists in pursuit of knowledge has always been a thorny one.

In 1762 when Dr. Richard Walker, Vice-Master of Trinity, bought a large part of Austin Friary for a botanic and physic garden, some of the "Great House" belonging to it was used as a botanical laboratory and lecture room. This house had been bought shortly after the dissolution by John Hatcher, who became Regius Professor of Physic in 1554. It was then an extensive building full of old monastic furniture and tapestry. Here he lived in princely magnificence until his death in 1586-7. Yet he made his own lozenges and had his own shop in Bene't Street, which ironically enough must have been on the same site as the present Culpeper shop, devoted to the herbalist cult. For it was Nicholas Culpeper, a Cambridge man, who inculcated that hostility to medicine still manifested by his disciples by his dictum: "The Colledg of Phisitians are too stately to learn and too proud to continue." For a time after Hatcher the premises had been used by John Buck for the University Printing Press, and it was due to the example of William Heberden that a botanic garden was instituted here. Dr. Walker wrote: "About 15 years ago the learned physician, Dr. Heberden was so kind as to oblige the University with a course of Experiments upon such plants as he then found amongst us in order to show their use in Medicines. This was entering into the practical and principal part of Botany to which we had been strangers. . . . But this Doctor's great Abilities in his profession soon after called him from us, much lamenting the want of a Public Garden, furnished with a sufficient variety of Plants for making the like experiments.

"These considerations, particularly Dr. Heberden's most useful attempt, put the present Vice-Master of Trinity College upon finding a proper situation for such a garden."

In 1832 the Botanic Garden was moved to the outskirts of Coe Fen, and the old site was gradually built over by University laboratories. Only the Friary Cafe at the corner of Free School Lane recalls the site of the old Augustinian splendour.

John Addenbrooke who founded the hospital known by his name, entered St. Catherine's Hall, as it was then called, in 1697, where he was successively scholar, Fellow, Prelector, Bursar and Tutor. He must have been a rich man, for he lent very considerable sums

of money towards the building of the College Chapel. There is no record of his taking his M.B., but he proceeded to the M.D. in 1710. In the following year he married the Master's niece, Miss Fisher, resigned his Fellowship and gave his medicine chest and books to the College library. A description of that chest has been given before this Section by Dr. A. W. Langford. Addenbrooke went to Caen in Normandy and took another M.D. there. He practised first in London and then at Buntingford, where he died in 1719; he was buried in the College chapel. He left his money to found the Hospital and his lands to some relatives. He had no children. There is only one surviving work of his, which was published while he was practising in London—an essay against Free Thinking, which has been described as "forceful but obscure". That I can well believe for a letter hanging framed in the hospital in which he complained of some breach of etiquette on the part of a professional colleague is couched in terms which are quite incomprehensible to me. In the Cole MSS. at the British Museum there is a letter from Mary Collis who looked after him in his latter days. She describes him as "a tall thin man, skilled in necromancy", who foretold the hour of his death which happened within five minutes of the predicted time; in this resembling Caius. He had all his manuscripts burnt in the courtyard of his house shortly beforehand. Mary Collis says he had "many oddities and [was] supposed at times to be insane".

His bequest of £4,000 being inadequate for the purpose he intended, the money was allowed to accumulate until 1766, when an appeal for subscriptions was started on May 1, which enabled the Hospital to be opened at Michaelmas of the same year. Even then it was very restricted for funds until more legacies fell in, particularly that of Mr. John Bowtell in 1813. Its successful modern developments lie outside my present topic.

I now come to the most important figure in eighteenth century Cambridge medicine, William Heberden. He was the first man who tried to rationalize pharmacology and materia medica, while in clinical medicine he insisted on direct observation without slavish adherence to tradition. He entered St. John's College in 1724 at the early age of 14, subsequently becoming a Fellow. He resigned his Fellowship, however, as soon as he could afford to do so, in order to allow someone poorer to take his place. He gave an annual course of lectures for ten years, during four of them as Linacre Lecturer. Several of his students rose to positions of distinction. He exposed the legend of that famous antidote, the Theriaca Mithridates. This proved to be a very trivial mixture of 20 leaves of rue, 1 gr. of salt and two dried figs; and Heberden infers that even if Mithridates had ever used it, which he doubted, his escape was less owing to the strength of his antidote than to the weakness of the poison. Yet by the time of Celsus a farrago which went by the same name consisted of 38 simples, and by the eighteenth century contained 70 ingredients. This was the kind of nonsense against which Heberden waged continual war; he ridiculed the stories about poisons concealed under the stone of a ring or emanating from perfumed gloves and letters.

His *Commentaries* strike an entirely different note from that of most contemporary medicine. Although not put together until he was 71 he tells us that they were prepared from notes collected at the bedside and revised every month in a light of fresh cases, but without borrowing from other writers. He stated in the preface that: "I am willing to employ the remainder of my days in teaching what I know to any of my sons who may choose the profession of physic; and to him I desire these papers should be given." As is well known his second son, also a William, became a highly successful physician. The sceptical turn of mind previously shown in his lecture on toxicology reveals itself again and again in these commentaries. Here are some examples: "Many physicians appear to be too strict in the rules of diet and regimen"—a remark which was made a century later by Sir William Roberts and is still applicable to-day. "The difficulty of ascertaining the powers of medicine", he asserts, "must have been felt by every physician and no aphorism of Hippocrates holds truer to this day than that in which he laments the length of time necessary to establish medical truths and the danger of our being misled even by experience." Again, "very few remedies have justified promises. However, the title of 'specific' may be justly claimed by Peruvian bark for ague, quicksilver for venereal disorders, sulphur for the itch and perhaps opium for some spasms. Besides these it may be doubted whether ten others have on any good authority been confirmed to be specifics". Thus "we have the misfortune to have innumerable remedies for the worm, this being pretty generally a sure sign that we have not one upon which we can with certainty depend". On gout he is entertaining and well ahead of his times. He says: "people are neither ashamed nor afraid of the gout, but rather ambitious of supposing that every complaint arises from a gouty cause and even try to contract it by means which happily for them are generally ineffectual . . . the belief that it is antagonistic to other diseases is fallacious." It will be remembered that Heberden's friend, Samuel Johnson, was cheered up when told by a Dr. Mudge that gout would be antagonistic to his palsy! To continue:

"the criteria of suppressed gout are very obscure. Hardly any of them give us ground to suspect it when there are no signs of history of articular gout. . . . The belief that strong wines and in no small quantity are beneficial for gout arises not so much perhaps from a reasonable persuasion of its truth as from a desire that it should be true because they love wine."

He attributed the value of the treatment at Bath to the change of surroundings and habits and to the suspension of business and cares rather than to something subtle in the waters.

He was more sceptical than Stephen Hales and David Hartley as to the value of Mrs. Joanna Stephens' notorious soap leys cure for the stone and records the case of a man who took ½ oz. of this nauseous draught almost daily for ten years. At the post-mortem one kidney was full of stones and there were two in the bladder. He tested the effect of soap leys *in vitro* on gall-stones, with a negative result and comments that "there is very little likelihood of their being able to do more in the body than out of it".

On pulmonary tuberculosis he remarks: "I have not seen proof enough to say that the breath of a consumptive is infectious and yet I have seen too much appearance of it to be sure that it is not." As to its treatment by a sea voyage which lingered in fashion until nearly the end of the nineteenth century, he is non-committal: "I can go no further in its commendation than to say consumptive patients have borne it well." But he believed in fresh air: "No cordial is so reviving and many persons have been stifled in their own putrid atmosphere by the injudicious."

Sydenham had said that jaundice might be due to hysteria on which Heberden comments: "No reasonable deference to this accurate observer can make anyone very much doubt of his having been mistaken." Yet that same mistake was copied into some of the textbooks still in use in my student days. It is curious that he should have been sceptical about the association between diabetes and carbuncle, but still more curious that he should say "diabetes is a complaint which happily occurs but seldom . . . I have scarce had the opportunity of observing 20 cases". But he is clear that it was "the symptom of some other distemper and not of kidney disease". Sometimes he adopted an aphoristic style; thus of autonomous depression, he said: "It appears to be a misery much harder to be borne than most other human ills & makes every blessing tasteless & unenjoyable." Of the idea that epilepsy was likely to cease at puberty he wrote: "I should think [it] was founded on theory or in the hopes of the physician rather than on fact." On venereal diseases he commented: "Interested persons have endeavoured to exaggerate [the patient's] fears in order to make an advantage of them by the sale of their silly books and insignificant medicines." Again, "It is an inveterate opinion which my experience has uniformly contradicted that madness is influenced by the moon". "Palpitation of the heart in many instances arises from causes too fatal to admit or too frivolous to stand in need of a cure." "Lord Verulam blames physicians for not making euthanasia a part of their studies; and surely though the recovery of the patient be the grand aim of their profession, yet where that cannot be obtained they should try to disarm death of some of its terrors." His teaching was by no means simply negative. Some of his original observations now clearly recognized were forgotten for many years; thus he described dyschezia, as it is now called, and realized the connexion between fistula-in-ano and pulmonary tuberculosis. He knew that asthma was in many instances due to a nervous disturbance and he described the emphysematous bullæ that might result. "A little grume of blood", said he, "often forms the nucleus of a stone." He described the post-herpetic neuralgia of elderly patients and recommended sulphates for dysentery (which in this country would presumably be bacterial). Yet of all the wit and wisdom of these commentaries only one thing is generally remembered, his description of the nodes which still go by his name. Nevertheless, he does not appear to have attached much importance to them himself, for this is all he has to say on the subject: "What are these little hard knobs about the size of a small pea, which are frequently seen upon the fingers, particularly near the top, near the joint? They have no connection with the gout, being found in persons who have never had it; they continue for life and being hardly ever attended with pain or disposed to become sores, are rather unsightly than inconvenient, though they must be some little hindrance to the free use of the fingers."

In 1768 he gave the first real account of angina pectoris to the Royal College of Physicians in a paper entitled "Some Account of a Disorder of the Breast", which was based on 20 cases. Besides his lectures and his commentaries his principal literary efforts were directed towards urging the College of Physicians to establish Medical Transactions. The first of these appeared in 1767, but they only ran into three volumes. In addition to several original contributions he sketched out an admirable preface from which I may make the following quotations. "By attentively observing nature itself a greater progress has been made during the last century than had been till that time from the days of

Aristotle." Speaking of the importance of forming one common stock of knowledge, he said: "It is high time that this should be done as physicians have . . . fully run the round of commenting on the ancients and contriving theories and teaching systematical doctrine. . . . Some physicians still choose to wrangle about the meaning of the ancients rather than to consult nature herself . . . notwithstanding all that Bacon and Harvey and Newton . . . have witnessed against this ancient veneration. . . . In that sort of knowledge which depends wholly on experience, the latest writers must in general be the best. . . . The ancients are in reality very little read and attended to by practitioners, though the fashion of quoting and recommending them be still prevalent", and finally, "it were to be wished that writers would not confine themselves to relate only their successful practice but would have the courage to tell us the ineffectual and hurtful." I think the character of the man stands out clearly from his writings. For those who scoff at the whole of eighteenth century medicine I recommend reading the works of Heberden.

After taking his M.D. he practised in Cambridge for about ten years during which time, in 1741, the Regius Chair fell vacant. As already stated Russell Plumptre, unfortunately as it seems to me, was appointed. Whether Heberden desired the post is unknown but I agree with Sir Humphry Rolleston that had he been appointed he would probably have brought about a new birth of medicine in Cambridge more than a century before it actually took place. As it was, he moved to London in 1748 having been elected F.R.C.P. two years earlier. He had apparently collaborated with Henry Plumptre, the father of Russell, in preparing a new edition of the London Pharmacopœia. From this many useless drugs were deleted, but in some respects the purge was too drastic and several useful drugs had to be reinstated subsequently. Perhaps we may see Heberden's sceptical mind at work here. In 1749 he was elected F.R.S., delivered the Goulstonian Lectures and in the following year the Harveian Oration. Ten years later he gave the Croonian Lectures. But his heart seems always to have been in Cambridge and he often expressed a desire to return thither. On this point there are two different interpretations; Munk says practice came so slowly in London that Heberden thought he had better return, but his son's brief memoir gives no hint of this and certainly later on it was from his patients that the plea came for him to remain in London. Indeed although he declined the post of Physician to the King his practice became very large indeed. However, some support is given to Munk's view by the fact that he did not marry until he was 50. His wife was Mary Wollaston, a member of a brilliant family. By her he had five sons and three daughters. His second son, also named William, who became Physician-in-Ordinary to King George III and Queen Charlotte, declined a Baronetcy, but I do not know whether, like a physician of a later age, he asked for a fur coat instead! William Hyde Wollaston was a nephew of the elder Heberden; trained as a physician, he abjured practice as "mental flagellation" so anxious was he about his patients. Until he discovered how to make platinum malleable he was very badly off. After that he had a prosperous career in science.

Among Heberden's friends were Cowper the poet, Bishop Warburton the truculent critic, and especially Doctor Samuel Johnson. Boswell said that "Johnson had in general a peculiar pleasure in the company of physicians", but Heberden seems to have been his favourite. When Johnson had his attack of palsy, with aphasia but not accompanied by agraphia, in June 1783 he urgently wrote for Heberden and Brocklesby to come and see him. It is satisfactory to record that he had recovered his speech sixteen days later. Subsequently he wrote to Brocklesby, "tell Dr. Heberden that in the coach I read Ciceronianus, which I concluded as I entered Lichfield". So they were evidently in harmony over their literary interests. Heberden, Brocklesby, Warren and Butter all attended Johnson in his last illness without any fee, and in his will he asked each of them to take a book "at their election" from his shelves as a memento.

Heberden's sceptical attitude of mind did not extend to religion. On the death of a certain Dr. Conyers Middleton whose orthodoxy was much suspect, his widow consulted Heberden about the publication of a manuscript he had left on the inefficacy of prayer. Heberden said that though it might be worthy of her husband's learning, it would be injurious to his memory. But as it appeared that a publisher would give £150 for it, he bought it from her for £200 and then burnt the manuscript.

In his 70th year he decided to restrict his practice, so he bought a house near Windsor where he resided in the summer but practised in London during the winter for several years longer. He was a great walker until his 86th year, when he met with an accident which disabled him for the rest of his life. Yet when he was nearly 90 he said he did not know that he had ever passed a year more comfortably than the last. His mental power and memory remained unimpaired to the end and he was quoting Latin within forty-eight hours of his death which occurred peacefully and painlessly in 1801 in his 91st year. Thus ended a singularly complete life. His friend Dr. Macmichael has left a

glowing tribute to his personal character and charm in which he bears testimony to the "cheerfulness and serenity of his latest age". The impression left on my mind from the various records of his life I have read is that few physicians have been so greatly admired and beloved.

The most distinguished of Heberden's pupils was Robert Glynn who spent nearly all his long life within the precincts of the University. Glynn came from Eton to King's College in 1737, where he subsequently became a Fellow. After obtaining his medical degree he practised for a short time in Richmond, Surrey, but soon returned to Cambridge, where he practised until his death in 1800, from his rooms in College. Being left money by a relative he assumed the additional surname of Clobery, but was usually still referred to as Glynn. Munk said of him that "his life was one uniform course of integrity and benevolence. . . . Of long and distinguished celebrity in the University of Cambridge . . . this venerable philanthropist continued to enjoy to the end of his days the heartfelt reverence and affection not only of the middle-aged and advanced in years but also of the young". He was physically so ugly that it was said some patients were frightened of him at first, but not for long, and an illness he had was jokingly attributed to his catching sight of himself in a mirror. His eccentricities became famous in Cambridge. Among other things he had a detestation of opium. Once he said to a colleague: "I am going to be very ill and commit myself to your care, but on no account give me that vile drug opium or any preparation of it." On his recovery he enquired whether his friend had complied with his request or whether he had given him opium. "If I had not", was the reply, "you would not have been here to ask the question." When Russell Plumptre died in 1793 Pitt offered the Regius Professorship to Glynn who declined it on account of his advanced age, so Sir Isaac Pennington was appointed.

Glynn died in College aged 81, and according to his expressed wish was buried privately in the Chapel between 10 and 11 at night. But public feeling demanded some more eminent mark of respect and Dr. Mansel, Master of Trinity and then Vice-Chancellor, announced his intention of proceeding with Dr. Glynn's friends and relations on the following Sunday from Trinity to Great St. Mary's to hear a Memorial Sermon, and a large procession accompanied him. Glynn bequeathed the bulk of his property to King's College and is commemorated by a tablet on the south side of the Chapel.

These two scholar physicians, Heberden and Glynn, teacher and pupil, and life-long friends, must have been a gracious influence in Cambridge at a time when the University was largely sunk in sloth and indifference. They were true to the highest traditions of their profession, cultivated both the art and science of medicine and were rewarded by the admiration of their colleagues and the devotion of their patients.

I now come to a man of a very different type who had considerable importance in eighteenth century Cambridge. John Woodward, admitted to Pembroke by incorporation in 1695, who made the famous collection of fossils which commanded Whewell's admiration and who endowed the Chair of Geology which goes by his name, was also an indifferent and quarrelsome physician. He had been elected a Fellow of the Royal Society in 1693, but was expelled in 1710 for conduct unbecoming a gentleman. Sir Hans Sloane was reading a paper when Woodward made some grossly insulting remarks and not for the first time. He refused to apologize and expulsion followed. Sir Isaac Newton was in the Chair and when it was pleaded in Woodward's favour that he was a good natural philosopher, Newton remarked that in order to belong to that Society a man ought to be a good moral philosopher as well. Woodward brought an action for reinstatement, but without success. He next became notorious for his controversy with Richard Mead and John Freind on the treatment of smallpox. Mead was then at the height of his fame; his house in Gt. Ormond St., which afterwards became the Hospital for Sick Children, was crowded with books and works of art, and here he entertained in right princely style. He resented Woodward's attack with the air of a St. Bernard faced by a mongrel puppy. Encountering one another at the gate of Gresham College, each drew his sword but Woodward stumbled on the steps and fell. "Take your life", said Mead contemptuously; "anything but your physic", was the retort. Freind, as his political record shows, enjoyed disputes and continued his ridicule of Woodward, until Henry Plumptre, of whom I have already spoken, lampooned them both in his "Serious Conference between Scaramouch and Harlequin". Even Woodward's geological theories were disputed by John Arbuthnot who was granted the M.D. in 1705. Arbuthnot though in active practice and the favourite physician of Queen Anne, is better known as a writer and the intimate friend of Pope and Swift, who formed the Scriblerus Club with him. They published "The First Book of Martin Scriblerus" but did not continue it because of the mourning for Queen Anne. Both the Dunciad and Gulliver's Travels were originally designed to form part of another volume.

Those interested in figures may care to know that during the eighteenth century 608

persons were admitted to the Royal College of Physicians as Fellows, Licentiates or Extra-Licentiates. The two latter classes were not generally graduates of Oxford or Cambridge. The total number of Cambridge men admitted was 120, of whom 21 had become members of the University by incorporation or by Royal Mandate. I will refer briefly to some of those physicians whose names are of general interest, whether their work was mainly in Cambridge or, as was more usually the case, outside.

The most extraordinary medical alumnus of eighteenth century Cambridge was Thomas Dover, who despite his remarkable exploits was a friend of the great Sydenham. Lord Moynihan once gave an interesting lecture on "Truants from Medicine"; surely no one was ever such a startling truant as Dover. He was the son of Captain John Dover (one of Prince Rupert's officers) and after matriculating at Magdalen, Oxford, migrated to Caius College, Cambridge, in 1686. After obtaining his M.B., he practised in Bristol, where he became fascinated by shipping. Then, like Dr. Livesey of Treasure Island, he took to buccaneering! In the course of his voyages with Captain Woodes-Rogers, they touched at the island of Juan Fernandez in 1708-9 and rescued the original of Robinson Crusoe, the marooned Alexander Selkirk. Next they took a town in Peru by storm and a few months later captured a valuable prize—a ship of twenty guns and 109 men. Dover transferred to this ship, with Selkirk as Master; they reached England again in 1711, and Dover quietly resumed his practice in Bristol, becoming so successful that he removed to London in 1721 where he was admitted L.R.C.P. His fondness for prescribing mercury as well as his hasty temper led to his being nicknamed "the quicksilver doctor", but his principal medical claim to fame is his well-known powder. Munk says that nothing is known of his latter end, but Dr. J. A. Nixon has shown that he retired to the beautiful mansion of Stanway House in the Cotswolds, where with his friend Robert Tracy, he spent the closing years of his life, dying in 1742, aged 80. His family had long association with the Cotswolds, and his grandfather founded the famous Cotswold Games. Dr. Nixon calls attention to the interesting fact that Selkirk after returning with Dover, handed over his papers to Daniel Defoe, who had several cousins at Caius.

There are some other survivors from the seventeenth century who call for a passing notice: Clopton Havers of St. Catherine's left without taking a degree, but was famous for his description of the architecture of bone, which is still kept in mind by the name "Haversian canals". Nehemiah Grew was much more important as a botanist than as a physician, but he was the first to isolate sulphate of magnesia from Epsom waters. Sir Samuel Garth of Peterhouse took an active part in the life of the College of Physicians, but he is better remembered as a writer and a member of the Kit Kat Club.

When I was Second Censor at the College of Physicians, I was faced at the meetings of the Board by a crude, glaring portrait of Edward VII from the brush of Luke Fildes, but when I became Senior Censor, I sat on the other side of the table and was refreshed by the sight of three fine portraits—William Pitcairn by Joshua Reynolds, David Pitcairn by Hoppner, and perhaps best of all, Richard Warren by Gainsborough. Richard Warren was born at Cavendish, the son of the Archdeacon of Suffolk who was a leading antagonist of Bishop Hoadly in the Bangorian controversy. The son entered Jesus College in 1748, and after becoming fourth wrangler, was elected to a Fellowship. Dr. Peter Shaw, an eminent London physician, placed his son under Warren's tuition at Jesus, and liked the handsome young man so well that he encouraged him to take up medicine which he did, and married Shaw's daughter as well. He rapidly became very successful, and was Physician to George III. An able and delightful man, he was one of the first to discard the pompous manner hitherto considered appropriate to the physician of the gold-headed cane epoch. Perhaps his suavity of manner encountered a shock when in his usual style having said to Dr. Johnson he hoped he was better, he was gruffly told: "No Sir; you cannot conceive with what acceleration I advance towards death." For he may have remembered that Johnson had previously said: "Of all lying I have the greatest abhorrence [of telling a lie to a sick man for fear of alarming him] because I believe it has been frequently practised on myself." Warren's practice was said to have brought him £9,000 a year, and he certainly left £100,000.

David Pitcairn was the son of Major Pitcairn who was killed at the battle of Bunker's Hill. His Uncle William, President of the Royal College of Physicians and Physician to St. Bartholomew's Hospital, paid for his education and entered him at Corpus Christi College where he became M.B. in 1779. In the following year he became Physician to St. Bartholomew's on the resignation of his uncle. A contemporary said of him: "His countenance during youth was a model of manly beauty, and even in advanced years was accounted remarkably handsome." He died, not at an advanced age, but when he was 59, and was buried in the church of St. Bartholomew the Less in the same vault as his uncle and father. The memory of the Pitcairns is kept in mind at Bart's by the ward named after them. I do not know whether they were related to Robert Pitcairn, the midshipman

who first sighted the island now named after him, which became the home of the mutineers of the Bounty. Robert was lost at sea aged about 23.

Finally I come to the somewhat enigmatic figure of William Stukeley. It not infrequently happens that attached to a circle of brilliant men one finds an adherent who clearly is not of the same calibre in character or attainments. Yet the circle appears to do more than merely tolerate him. Perhaps he is an agreeable companion, or had merits which escaped his biographers, or perhaps the great appreciated the incense offered by the lesser light. Of this Boswell is the outstanding example, and I think William Stukeley of Corpus must have been of that type. He was certainly a friend of Stephen Hales and he was a Boswell to Isaac Newton. He helped John Ray in his catalogue of Cambridgeshire plants. Entering Corpus Christi College in 1708 he studied chemistry under Vigani and anatomy under Rolfe, though as I have said since Rolfe was subsequently deprived of his office for neglect of his duties it is doubtful if Stukeley learned much from him. That he was interested, however, is shown by his habits of dissecting cats and dogs in his college rooms. Dr. Clark-Kennedy in his recent paper on Stephen Hales before this Section certainly gave us a vivid account of the lively scientific interest he roused in the undergraduates at Corpus, and Stukeley's diary shows that he shared in this to the full. From Cambridge Stukeley went to St. Thomas's Hospital where he studied under the great Mead. He was elected F.R.S. in 1717, and in the following year he took a leading part in founding the Society of Antiquaries. He proceeded to the M.D. and became F.R.C.P. giving the Goulstonian Lectures with the spleen for his subject, and subsequently acted as Censor. His antiquarian researches included Hadrian's Wall, Stonehenge and Maiden Castle. It may be asked why with such a record I should be doubtful of his real merit. Certainly not because of his unconventional behaviour after he took orders; it may even be imputed to him for righteousness that on one occasion he postponed divine service for an hour to enable the congregation to witness an eclipse of the sun. Even Bishop Warburton who spared neither friend nor foe said of him that he was an honest and learned man, but then added that he was a strange compound of "simplicity, drollery, absurdity, ingenuity, superstition and antiquarianism". Gibbon said: "I have used his material and rejected most of his fanciful conjectures." Thomas Hearne described him as "very fanciful and a mighty conceited man". That he must have been very conceited is proved by the highly laudatory biography he wrote of himself in Master's History of Corpus in the third person, in which he attributed his lack of success as an author to the artifices of booksellers which prevented him from reaping the fruits of his labours. His reliability as a scholar may be gauged by his conviction that he had proved the identity of Bacchus and Jehovah. No wonder Gibbon could not accept his conjectures! I think I am justified in concluding that his ambitions exceeded his intellectual equipment and that his scientific friends perhaps found him more amusing than inspiring.

In looking back from this present Age of Violence to the so-called Age of Reason it is easy but erroneous to form judgments in the light of subsequent events. It would, however, be generally admitted that the effect of Newton upon its thought was enormous. A. N. Whitehead makes this interesting comment: "Gibbon . . . was the incarnation of the dominant spirit of his own times. In this way his volumes also tell another tale. They are a record of the mentality of the 18th century. . . . This silver age . . . was oblivious of its own imminent destruction by the impact of the Age of Steam and of Democracy. . . . Thus Gibbon narrated the Decline and Fall of the Roman Empire and exemplified the prelude to the Decline and Fall of his own type of culture."

BIBLIOGRAPHY

BOSWELL, JAMES. Life of Dr. Samuel Johnson. *Passim.*
CLARK-KENNEDY, A. E. (1929) Stephen Hales, London.
Dictionary of National Biography.
HEBERDEN, WILLIAM (1801) Commentaries, edited by William Heberden the Younger, London.
LANGFORD, A. W. (1935) *St. Catherine's Society Magazine,* 43.
—— (1936) *St. Catherine's Society Magazine,* 26.
—— (1937) *St. Catherine's Society Magazine,* 61.
MASTERS, W. (1753) History of Corpus Christi College, Cambridge, 196, 381.
MULLINGER, J. B. (1901) College Histories, London.
MUNK, W. (1878) The Roll of the Royal College of Physicians of London, 2.
NIXON, J. A. (1909) *Bristol med.-chir. J.,* 27, 31.
—— (1913) *Proc. R. Soc. Med.,* 6, Sect. Hist. Med., 233.
ROLLESTON, Sir H. (1932) The Cambridge Medical School, London.
WHITEHEAD, A. N. (1942) Adventure in Ideas, Harmondsworth.
WILLIS, R., and CLARK, J. W. (1886) Architectural History of the University of Cambridge, London.

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[*October* 26, 1943]

Mental Health

PRESIDENT'S ADDRESS

By GEOFFREY EVANS, M.D., F.R.C.P.

Physician, St. Bartholomew's Hospital

DR. EVANS in his opening remarks outlined his thesis in the following terms. Human nature is as yet incompletely understood. The crux of the problem is the human mind. Science has established the organic unity of the universe. We can look back, not to the beginning, but according to Professor Jeans, to something like 3,000 million years ago, when matter in a form smaller than atoms was more or less evenly distributed through space. The universe was in darkness and its temperature was about that of melting ice. Out of this were created the heavenly bodies and the Milky Way, the sun and its planets, this world of ours and its moon—and all this by the operation of natural laws. There is a pattern in everything, from the infinitely small, such as atomic and molecular form, and nuclear structure to the vastly great: it would seem that our sun with its planets is but a part of a pattern on a scale magnificent, and that ours is not the only planetary system in the universe.

Dr. Evans visualized a Vital Impulse existing at least in all matter inanimate as well as animate. He referred to the ceaseless movement within the atomic structure of even cold steel—as postulated by science. He realized this as expressing itself in motion, in continual change; in ordered elaboration of form (which is evolution), working itself out in animate nature in growth and reproduction, finding for itself further expression in the mind and instincts of animals and man, and in the present achieving its highest expression of activity at one and the same time in the instinctive feelings of man and in his spiritual aspirations and abstract thought. In terms of these two paths of expression of the Vital Impulse, which he called the Sensuous and Super-sensuous Spheres, Dr. Evans presented the Pattern of the Mind.

THE SENSUOUS SPHERE

The human body, Dr. Evans said, in its structure and function conforms to this universal tendency to pattern. And as there is a basic pattern to the structure of the brain, so Professor Jung has put forward the conception of a basic pattern in intellectual activity, the "universal collective psyche." He finds evidence of this in, for example, the extraordinary similarity of the myth-forms of aborigines. But in the understanding of the mind we are concerned only with function and this function is feeling.

Humanity lives under the delusion that it is acting on a rational basis, whereas its actions are largely determined by instinctive feeling. The primitive instincts which are common to animals and man are those of Self-preservation, Creation and Destruction. These are the basic components of the human mind. It is significant that each of them is associated with the name and doctrine of a well-known experimental psychologist. Adler interpreted psychoneurosis in terms of repression of the instinct of self-preservation, the ego instinct, the will to power. Freud was the champion of the creative instinct, which he realized chiefly in terms of the sexual impulse, and its over-riding expression in the gratification of this instinct. These two instincts have this in common, the former the survival of the individual, and the latter the survival of the

human race. Together they have up to date proved stronger than the instinct of destruction. The name of Stekel is especially associated with the instinct of destruction. He speaks of "two eternal forces controlling man's psychic life, hate and love: or, better expressed, the life impulse and the death impulse". He seems to give preference to the destructive instinct when he says: "Hate is the really great motive power of all that happens." It is fair comment to observe that we humans can create ideas only from our own experience, a fact which led Jung to observe that whereas Adler was an introvert Freud was an extrovert, and that on this account they offered a different interpretation of the same problem.

To the three basic instincts, self-preservation, creation and destruction, which are the essential components of the human mind, must be added the herd instinct. Trotter regarded the herd instinct as an acquired function of the mind. To his interpretation the mind of the gregarious animal "possesses a specific sensitiveness to external opinion, and the capacity to confer on its precepts the sanction of instinctive force". He further elaborates this conception by remarking that "the repressing forces (of herd opinion) become actually constituent in the child's personality, and as much a part of his being as the egoistic desires with which they are now able to contend on equal terms". These four instincts are the chief components of the core of the human mind. They are the sensuous sphere.

Self-preservation.—Infancy and childhood are, as one would expect, largely animated by the instinct of self-preservation, and so for the fullest development of personality and character a child requires above all things security and love. In adult life the impulse of creation tends to supersede the instinct of self-preservation, and self-sacrifice is born. But for creation too some measure of security is required, and for its greatest achievements some measure of isolation too. These things are common knowledge, and establish the fact that the home and home life is the essential unit of a society that has reached the highest level in the evolution of mankind. The Church, politicians, educationists and doctors, must make this the foundation of their plans for mental health. We must be slow to interpret self-interest in terms of selfishness. Self-interest determines self-preservation. It is in itself a contribution to democracy, because if every member of a democratic state were self-dependent what a surplus of power and energy there would be for creation! Self-interest too is required to provide the material background of a home, and to maintain its existence. Self-interest, like every other instinct, requires control, and is only harmful when it expands to the detriment of others and of the State. In itself, however, self-interest is not sufficient as a prime objective in life. However successful a man may be in the acquisition of financial fortune and worldly position it does not satisfy the needs of his human nature, and such a man frequently devotes part of his fortune or a part of his life to some creative activity, to the service of others, or to the State.

Creation.—Creative activity in its widest sense is the real purpose of life. Women in bearing children create life, men create things, concrete and abstract. It is to the restriction and limitation of creative activity that much mental ill-health is due. In the case of married women the absence of children is a well-established cause of married unhappiness, and it is our experience as doctors that an only child, or perhaps only two children, may not satisfy the needs of human nature, at least in later life. Creative activity demands self-sacrifice. A woman may lose her life in childbirth, and is ready to sacrifice herself for children. The creative activity of a married woman is not, of course, to be measured by the number of her children. Generally speaking a woman is ultimately responsible for the activities of a man. She may find the outlet for her creative function in his life's work. She may indeed be responsible for its direction and for his achievement. A man must be ready to sacrifice himself to his work or for an idea. Self-preservation gives way before the demands of creative activity in both men and women. Before the war creative activity was at a discount. When it was possible people looked forward to living on income, inherited or earned, and idleness was encouraged by the provision of pensions at an ever earlier age. Families were becoming smaller, and the birth-rate was falling. A vast number of men and women were occupied in administration, supervision and tending machines. The machines did the creative work. An interest in life was found in playing the gallery game, in cinemas, horse and dog racing, in watching cricket and football matches. The purpose of life, even if the occupation was in creative activity, was holidays or leisure away from work. The war has contributed to show the poverty of all this. In spite of stress and strain, discomforts and anxieties, the health of the community has improved with war, and this may be due to the outlet provided for the basic needs of human nature by the opportunity for creation and destruction on a great scale. In our planning for

mental health in the future, ample opportunity for creative impulse must be found by the encouragement of home life and larger families, and by finding opportunity for creative activity in art and literature, in allotments and gardens, and other such occupations, for those who cannot find expression for their natural instincts in their daily work. The opportunity for creative activity is not open to all, nor has everyone the energy or courage for its undertaking. Service amply takes its place. This service may be performed for an individual, for an institution or for the State. Service has another advantage. Most people require a constant supply of appreciation for their mental health and happiness. This applies equally to women and to men. For women personal service contributes best to mental health. Men, more easily than women, are able to satisfy their needs in the service of an institution, an idea, or some abstraction, because a man gets his appreciation from the woman to whom he is attached. Both in doctoring and nursing, service is rewarded by generous appreciation from those to whom service is given. It follows, then, that for the attainment of mental health when there is no opportunity for creative activity an opportunity for service must be found to take its place.

Destruction.—In infancy, childhood, adolescence and adult life, the instinct of destruction is always present, and of quite unrealized strength. The instincts of self-preservation and creation up to the present time have beaten the spirit of destruction by but a narrow margin, but unless the strength of the destructive instinct is fully realized human nature will destroy itself before long. In general terms the instinct of destruction is stronger in men than in women, and there are many occupations in which there are opportunities for its display. It would be shocking to detail these occupations in their great variety, and it would be denied that the spirit of destruction is an animating impulse in their pursuit, but at least it will be agreed that demolition workers, butchers, timber fellers, and game-keepers, find some opportunity in their work for the outlet of this instinct. The reason that the spirit of destruction is not generally recognized, and indeed is regarded by so many with such horror, is because destruction is often associated with pain, although pain is only incidental to it; because too there may be a joy in the destruction of human life, and this is cruelty; also because like every other instinct it may be perverted, and the most fiendish actions of which humanity is capable will then result. Yet in itself Dr. Evans regarded destruction as natural and good, giving strength to character and combativeness to overcome evil. Uncontrolled destruction is alarming, and must be met and overcome by greater force, or even controlled by fear. This war is not, he thinks, "a sporadic outburst of barbarism"; it has its origin in the basic forces of the human mind. In generations to come it may be possible to deal with it by appeal to feeling in the super-sensuous realm, but this will not be in our time.

The herd instinct is all pervasive in human life. More of our actions and thoughts are due to others than we are ever aware of. Fashion in clothes is an obvious example. Fashion in thought and feeling is just as common. The present subordination and direction of all individual capacity to service of the State is determined by war, but over and above this the continental ideology of pre-war days, accentuated by war, is having a great and unsuspected influence on English thought. The partial isolation of our island home, which has contributed so much to British character and inventive genius, now runs the risk of being flooded by the fashion of continental thought, and against this danger to the independence of British outlook we must be prepared to defend ourselves when the war is over. Our individualistic outlook must be preserved if an endo-psychic conflict on a national scale is to be prevented, a conflict between the instincts of self-preservation and the herd. Such a conflict would sow the seed of widespread mental ill-health and could lead to revolution.

THE SUPER-SENSUOUS SPHERE

It is commonly imagined, Dr. Evans said, that in this sphere intellect and rational thought reign supreme, but as a fact both are coloured by emotion. Primitive impulses, that is the components of the sensuous sphere, still remain the basis of feeling and action. When the likeness of human beings to animals was first generally recognised, and when the doctrine of evolution made its first impact on scientific minds, there was a tendency to emphasize the likeness and to minimise the difference between man and beast. But as experience of life and people increases it becomes apparent that there is a general desire among individuals to do better and to be better, and this in the highest sense. It dawns on the observer that the determining difference between animals and man is the power of humanity to distinguish between good and evil. This is a great discovery, which gains in importance when it is realized that it has been known for centuries past. Aristotle, for instance, wrote:

"Nature, as we often say, makes nothing in vain, and man is the only animal whom she has endowed with the gift of speech. And whereas mere voice is but an indication

human race. Together they have up to date proved stronger than the instinct of destruction. The name of Stekel is especially associated with the instinct of destruction. He speaks of "two eternal forces controlling man's psychic life, hate and love: or, better expressed, the life impulse and the death impulse". He seems to give preference to the destructive instinct when he says: "Hate is the really great motive power of all that happens." It is fair comment to observe that we humans can create ideas only from our own experience, a fact which led Jung to observe that whereas Adler was an introvert Freud was an extrovert, and that on this account they offered a different interpretation of the same problem.

To the three basic instincts, self-preservation, creation and destruction, which are the essential components of the human mind, must be added the herd instinct. Trotter regarded the herd instinct as an acquired function of the mind. To his interpretation the mind of the gregarious animal "possesses a specific sensitiveness to external opinion, and the capacity to confer on its precepts the sanction of instinctive force". He further elaborates this conception by remarking that "the repressing forces (of herd opinion) become actually constituent in the child's personality, and as much a part of his being as the egoistic desires with which they are now able to contend on equal terms". These four instincts are the chief components of the core of the human mind. They are the sensuous sphere.

Self-preservation.—Infancy and childhood are, as one would expect, largely animated by the instinct of self-preservation, and so for the fullest development of personality and character a child requires above all things security and love. In adult life the impulse of creation tends to supersede the instinct of self-preservation, and self-sacrifice is born. But for creation too some measure of security is required, and for its greatest achievements some measure of isolation too. These things are common knowledge, and establish the fact that the home and home life is the essential unit of a society that has reached the highest level in the evolution of mankind. The Church, politicians, educationists and doctors, must make this the foundation of their plans for mental health. We must be slow to interpret self-interest in terms of selfishness. Self-interest determines self-preservation. It is in itself a contribution to democracy, because if every member of a democratic state were self-dependent what a surplus of power and energy there would be for creation! Self-interest too is required to provide the material background of a home, and to maintain its existence. Self-interest, like every other instinct, requires control, and is only harmful when it expands to the detriment of others and of the State. In itself, however, self-interest is not sufficient as a prime objective in life. However successful a man may be in the acquisition of financial fortune and worldly position it does not satisfy the needs of his human nature, and such a man frequently devotes part of his fortune or a part of his life to some creative activity, to the service of others, or to the State.

Creation.—Creative activity in its widest sense is the real purpose of life. Women in bearing children create life, men create things, concrete and abstract. It is to the restriction and limitation of creative activity that much mental ill-health is due. In the case of married women the absence of children is a well-established cause of married unhappiness, and it is our experience as doctors that an only child, or perhaps only two children, may not satisfy the needs of human nature, at least in later life. Creative activity demands self-sacrifice. A woman may lose her life in childbirth, and is ready to sacrifice herself for children. The creative activity of a married woman is not, of course, to be measured by the number of her children. Generally speaking a woman is ultimately responsible for the activities of a man. She may find the outlet for her creative function in his life's work. She may indeed be responsible for its direction and for his achievement. A man must be ready to sacrifice himself to his work or for an idea. Self-preservation gives way before the demands of creative activity in both men and women. Before the war creative activity was at a discount. When it was possible people looked forward to living on income, inherited or earned, and idleness was encouraged by the provision of pensions at an ever earlier age. Families were becoming smaller, and the birth-rate was falling. A vast number of men and women were occupied in administration, supervision and tending machines. The machines did the creative work. An interest in life was found in playing the gallery game, in cinemas, horse and dog racing, in watching cricket and football matches. The purpose of life, even if the occupation was in creative activity, was holidays or leisure away from work. The war has contributed to show the poverty of all this. In spite of stress and strain, discomforts and anxieties, the health of the community has improved with war, and this may be due to the outlet provided for the basic needs of human nature by the opportunity for creation and destruction on a great scale. In our planning for

It is in this sphere that religion plays its part. Science provides the basis for religious thought, as is of course to be expected, because intellect and rational thought reign in the super-sensuous sphere, though not supreme. Science realizes the organic unity of the universe. Motion is universal. In the infinitely small, electrons revolve round the nucleus of an atom: the earth revolves round the sun: the stars move in the heavens: there is continual change. The universe, it seems, has increased 100 times in size within the measure of calculable time. This movement, this change in the direction of ordered elaboration is evolution. Through it there is an all-pervading pattern. So much for science. Religion sees design in pattern. Just as science brings all measurable things into an organic unity or whole, so religion brings all these basic scientific conceptions into one conceptual whole. Religion, too, gives to all these thoughts and concepts a feeling tone, and this is the sensation peculiar to the super-sensuous sphere. Religion does more than this. It teaches mind control and concentration by prayer. It inculcates discipline of body and mind by religious observance. When to all this is added a firm belief in the beneficence of The All-pervading Power mortal man finds peace of mind. All this, or much of it, is the interest of religious bodies, and they must bestir themselves to provide the outlet for the vital impulse in the super-sensuous realm. Educationists and doctors can take a part by teaching how to harness thought and set it in the right direction. Tennyson said: "Think well—Do well will follow thought." Thought can initiate emotion. Thought can be thought-controlled. It can also be mind-controlled. In this doctors have their opportunity, for not only the attitude of the body, but also its physical condition, affects the mind.

Surgeon Captain Desmond Curran said mental ill-health, like mental health, was dependent upon general and social factors, largely or entirely outside medical control. Psychiatric practice in the Service was more dependent upon the possibility of manipulating the environment than was perhaps any other branch of medicine. The co-operation of the executive authorities was therefore absolutely essential and without this outside co-operation the psychiatrist could, by himself, do relatively little and for the very reason that psychiatry was the most personal branch of medicine. For the more a man was considered as a whole, the more important did his social relationships become, since man was a social animal.

All Service medicine was in a special way social medicine, for the Service doctor was required to answer, with no havering, social questions, such as was the man fit for duty, when would he be fit for duty and what sort of duty. A satisfactory answer to such questions was only possible if the psychiatric aspect of the case was also considered, no matter what the complaint.

The possibilities of treating neurotic cases in the Navy while still at duty were largely dependent upon the opportunities that existed for recommending, when necessary, restricted types of duty. The executive authorities were usually willing to accept psychiatric recommendations, although any attempt at medical dictatorship would (and he thought rightly) be resisted. They had the power to place men in a general medical category, such as shore service only, but only to make recommendations for their placement within that category. He thought this an important principle and was as it should be. For apart from other considerations, a lot of the success that was achieved depended upon powers of compulsion; and, except in certain restricted spheres, these were not best exercised by medical men. The compulsory powers that existed were of course essential for Service efficiency; but they were also of striking benefit to many of the men themselves, who were greatly helped by finding that, under pressure, they could do more than they thought, or would have done on their own initiative in civilian life.

For the early treatment of psychiatric cases in the Navy much depended upon the ordinary medical officers in ships and shore establishments.

Turning to the hospital arrangements, the success that had, on the whole, been achieved by the neuropsychiatric units that had been instituted in the main naval hospitals had been gratifying. It was important that psychiatry should develop in the closest possible relationship with general medicine and surgery, for the advantages were mutual, and the educational value not least for the psychiatrist.

What was achieved in the naval neuropsychiatric units would, however, be woefully incomplete without subsequent facilities for rehabilitation, preferably, if a man was fit enough for it, while still at some form of duty and under the supervision of one of the naval neuropsychiatric specialists working in the main naval depots. For those who were not fit enough for this, two types of rehabilitation units had been found desirable. One, for the better type of man, under purely medical management, the other, for the less good type of man, under executive direction, who could wield the compulsory powers that might be necessary.

This raised the question of what power was it reasonable to confer on doctors, and more particularly on psychiatrists, in order that they might implement what they thought proper. It could scarcely be argued that because social and economic factors had important medical implications they should therefore be regarded as a purely medical affair.

This problem of the psychiatrist's role of adviser and expert evidence, as opposed to executant and judge, might be illustrated by a brief consideration of a basic requisite for mental health, namely suitable employment.

of pleasure or pain, and is therefore found in other animals, the power of speech is intended to set forth the expedient and the inexpedient, and therefore likewise the just and the unjust. And it is a characteristic of man that he alone has any sense of good and evil, of just and unjust, and the like."

Both these distinctions are noted in the Book of Genesis. By eating the fruit of the tree of knowledge Adam and Eve learnt the difference between good and evil. The birth of language is recorded—"And Adam gave names to all cattle, and to the fowl of the air, and to every beast of the field." Professor Wilson in his book, *The Miraculous Birth of Language,* analyses the difference between the rudi-language of animals and the definite shape and individuality of human words, each invested with a definite limited arbitrary (or conventional) meaning. He argues that this differentiation of sounds which constitutes human language is the product of a mind which differentiates one object from another in space, and one event from another in time, in an explicit way beyond the scope of any animal. The next step in the evolution of the mind of man was the conversion of sound-symbols into form-symbols, in other words, the invention of written language. Man also differs from animals in his power to place things in time and space. A dog's idea of time is presumably limited by his lifetime, and his idea of space is limited by his experience of space. Man lives in a double world, the world he experiences and shares with animals, and a world he can imagine beyond the limits of time and space. Language alone expresses this double world of space and time in which man lives. It expresses the emergence of the human mind into the free sphere of conscious thought. Language provides the symbols by means of which the human mind registers its transference from the realm of the primitive senses to the realm of the imagination.

In this super-sensuous sphere of thought and feeling human beings conceive their standards of truth and justice and their ideals of honour, virtue and the like. It is in this sphere of idealism that human nature has reached its highest level on the winding stair of evolutionary change. We are led to believe that activity in this sphere is the highest expression of the purpose of life. This dual nature of man belonging at one and the same time to both sensuous and super-sensuous spheres must be completely realized if human nature is to be understood. In reaching out to the purest idealism the human mind cannot grow out of the primitive sensuous sphere, nor can it leave it behind. The mind is dyed with the instincts of self-preservation, creation, destruction and the herd. These instincts give feeling tone to the highest thoughts conceived in the super-sensuous sphere by the human mind.

MENTAL HEALTH

Mental health depends in some measure on adjustment to the surroundings as well as on the co-ordination and harmony in working of the components of the mind. There must be an opportunity for the expression of the vital impulse, and this will be in the direction of self-preservation, creation, or destruction, initiated perhaps, but certainly directed and controlled by the imaginative faculties of the super-sensuous sphere. A man's activities are the expression of the purpose of life, and the objective best contributes to mental health when it is outside himself and seems to the individual to be worth his while.

Mental ill-health is due to a failure of adjustment of the mind to its surroundings and to a disharmony or conflict in the working of the components of the mind. This disharmony may be due to an endo-psychic conflict within the sensuous sphere, or to a conflict between the sensuous and super-sensuous spheres. The explanation of mental ill-health in terms of conflict has been greatly exaggerated. In ordinary life and general medical practice the commonest causes of mental ill-health are lack of outlet, exhaustion, and frustration, and even when conflict results from defeat or frustration it is best resolved by acceptance, or it is often better sublimated by diversion and direction to the level of the super-sensuous sphere than by its analysis on the sensuous level.

The future of mankind depends on the development and growing power of activity in the super-sensuous sphere. And it is a power that must be expanded under discipline and control. It must be developed in conjunction with activity in the sensuous sphere. To develop it alone is to encourage mysticism, which from the point of view of mental health is a dangerous doctrine. A healthy mind is better cultivated by the development of human nature at the same time in its sensuous and super-sensuous spheres. It should be the objective of every man and woman, writes Professor Jung, "to stand with feet firmly planted in the ego-function, that is he (or she) must fulfil his duty towards life completely, so that in every respect he is a vital member of society".

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S.

[*November* 19, 1943]

Some Recent Studies and Investigations in Sterility

By ALBERT SHARMAN, M.D.

THE title of this paper indicates both the scope and limitations of the communication. I have selected for consideration certain aspects of the problem which I have been investigating over a number of years, together with some recent observations (I) on the estimation of tubal patency; (II) on anovular menstruation as assessed by endometrial biopsy; (III) on endometrial tuberculosis; and (IV) on the causation of tubal occlusion.

These observations are based on a consecutive and unselected series of 500 cases of primary sterility, with additional selected cases, the subject of particularized research.

I. *Recent Observations on the Estimation of Tubal Patency*

The methods employed have been (*a*) insufflation and (*b*) hysterosalpingography.

(*a*) *Insufflation.*—The total number of patients in the series, whose tubes were insufflated, amount to 480, of whom 232 had two or more insufflations. In most instances the test was repeated simply as a confirmatory procedure; in many it was done to compare the findings with and without anæsthesia; but in 22 patients, 6 or more insufflations were done to study the behaviour of patent tubes over a considerable period of time. The figures in this group are as follows:

6	insufflations	were	performed	in	11	cases
7	„	„	„	„	4	„
8	„	„	„	„	2	„
9	„	„	„	„	1	case
12	„	„	„	„	1	„
14	„	„	„	„	1	„
23	„	„	„	„	1	„
25	„	„	„	„	1	„

The total number of insufflations performed in the whole series is 1,003. For over six years the kymograph has been used in conjunction with tubal insufflation, and it may here be stressed that its value cannot be over-estimated. (Examples of kymographic tracings were shown.)

A study of the behaviour of patent tubes as revealed by repeated insufflations shows that under similar conditions, e.g. the constancy of the rate of the flow of the gas, there is a noteworthy constancy in the appearance of the tracings obtained. No great difference, either in the level at which patency is established, or in the appearance of tubal contraction waves is usually seen in any given patient when insufflation is repeated, even after several months. Increase in the rate of flow of gas may be followed by a marked increase in the patency-pressure level and by more active, deeper peristaltic waves; but this is not invariable. Around ovulation-time (presumptive) more active or more frequent peristalsis may be seen. This also is not invariable, and there is no indication that there is any constant close correspondence between the type of tracing obtained and the stage of the endometrial cycle. On the other hand repeated insufflations have shed some interesting light on the criteria of non-patency. The first point is that a single finding of non-patency is not reliable. This has been proved by the subsequent occurrence of pregnancy or by the occurrence of a characteristic kymographic tracing of patency (corroborated by the occurrence of shoulder pain or by the demonstration of pneumoperitoneum) or by hysterosalpingography. A study of this group (25 patients) may throw some light on this apparently anomalous finding, and may be of assistance in obviating a possible source of erro   The findings   ized as follows: (1) In 9 patients two tests on

OBSTET. 1

It was obviously so desirable to fit people into the jobs most suited to their capacity that there might be a danger of judgment being seduced by enthusiasm, both as to what could be claimed and as to what people would stand if they had any option. The claims that could be made at the present time about vocational selection and vocational guidance, although the war had demonstrated them to be quite real, should be duly modest. Many of the most important qualities shown in life were extremely difficult to assess beforehand and were not susceptible of measurement. Again test results possessed for many a peculiar seductiveness, since they were expressed in a numerical form; but the precision was often more apparent than real, since it was not always clear what was being measured or how what was being measured related to what was wanted, or even what indeed was wanted.

It might be submitted that the medical role was traditionally and properly one of restriction. It was not for the doctor to choose the football eleven, although he could say that a man was not fit to play. On the positive side he could also say that he could find no medical reason why the man should not play. But he could not reasonably claim to be elected a member of the selection committee merely because he was a doctor or even a psychiatrist. A knowledge of football was a more important qualification. It might be held that the same principle should apply in the case of vocational selection. In vocational guidance the problem was a different one, since for that the emphasis was laid primarily upon what would be best for the individual and not on what would be best for society or the group.

In problems which were not strictly medical, and the sick constituted the only quite specific sphere of medical responsibility, the best course seemed to be to put forward the facts as they appeared and also perhaps to advocate what action seemed appropriate, but to leave the ultimate decision to others.

Reserved views might also be held about mental hygiene propaganda. The less that was actually said about nerves in the Navy the better and the same possibly held true for civilians. There was perhaps something to be said for the view that people should be taught in the good old way that this life was a vale of tears and that consequently to feel uncomfortable or unhappy or frustrated was to be expected, was unlikely to be evidence of sickness, and seldom a good reason for giving up work. The realization of these truths might materially reduce the task of the psychiatrist.

The best contribution that the medical profession could make to mental health lay perhaps in their own better education, the need for which had been strikingly shown by the men passed fit for the Services in the war. Another clamant need was for better facilities for research into these most difficult problems. It was obvious that at least all the main teaching hospitals should possess a proper neuropsychiatric unit. Was social maladaptation by itself necessarily evidence of sickness? This depended upon the definition of terms. The simple view that a man was either a medical case not responsible for it and in need of medical treatment, or not a medical case and therefore responsible and not in need of medical treatment, was inadequate from the psychiatric standpoint.

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S.

[*November* 19, 1943]

Some Recent Studies and Investigations in Sterility

By ALBERT SHARMAN, M.D.

THE title of this paper indicates both the scope and limitations of the communication I have selected for consideration certain aspects of the problem which I have been investigating over a number of years, together with some recent observations (I) on the estimation of tubal patency; (II) on anovular menstruation as assessed by endometrial biopsy (III) on endometrial tuberculosis; and (IV) on the causation of tubal occlusion.

These observations are based on a consecutive and unselected series of 500 cases of primary sterility, with additional selected cases, the subject of particularized research.

I. *Recent Observations on the Estimation of Tubal Patency*

The methods employed have been (*a*) insufflation and (*b*) hysterosalpingography.

(*a*) *Insufflation.*—The total number of patients in the series, whose tubes were insufflated, amount to 480, of whom 232 had two or more insufflations. In most instance the test was repeated simply as a confirmatory procedure; in many it was done to compare the findings with and without anæsthesia; but in 22 patients, 6 or more insufflations were done to study the behaviour of patent tubes over a considerable period of time. The figures in this group are as follows:

6	insufflations	were	performed	in	11 cases		
7	„	„	„	„	4	„	
8	„	„	„	„	2	„	
9	„	„	„	„	1 case		
12	„	„	„	„	1	„	
14	„	„	„	„	1	„	
23	„	„	„	„	1	„	
25	„	„	„	„	1	„	

The total number of insufflations performed in the whole series is 1,003. For over si years the kymograph has been used in conjunction with tubal insufflation, and it ma here be stressed that its value cannot be over-estimated. (Examples of kymograph tracings were shown.)

A study of the behaviour of patent tubes as revealed by repeated insufflations show that under similar conditions, e.g. the constancy of the rate of the flow of the gas, the is a noteworthy constancy in the appearance of the tracings obtained. No great diffe ence, either in the level at which patency is established, or in the appearance of tub contraction waves is usually seen in any given patient when insufflation is repeated, ev after several months. Increase in the rate of flow of gas may be followed by a mark increase in the patency-pressure level and by more active, deeper peristaltic waves; but t is not invariable. Around ovulation-time (presumably) more active or more freque peristalsis may be seen. This also is not invariable, and there is no indication that the is any constant close correspondence between the type of tracing obtained and the sta of the endometrial cycle. On the other hand repeated insufflations have shed son interesting light on the criteria of non-patency. The first point is that a single finding non-patency is not reliable. This has been proved by the subsequent occurrence of pre nancy or by the occurrence of a characteristic kymographic tracing (corroborat by the occurrence of shoulder pain or by the demonstration of pneumoperitoneum) or hysterosalpingography. A study of this group (25 patients) may throw some light on tl apparently anomalous finding, and may be of assistance in obviating a possible source erro The findings may be summarized as follows: (1) In 9 patients two tests or

were performed; in 15 patients, three tests, two showing patency and one non-patency; in 1 patient four tests, three showing patency and one non-patency. Thus none of the patency cases showed non-patency more than once. (2) Anæsthesia was employed in 12 of the group when 1 insufflation showed non-patency. In a further 2, with anæsthesia patency was shown, but without it non-patency. The remainder (11) had no anæsthetic at any insufflation.

The conclusions that may be drawn from a study of this small group are (1) in cases of tubal patency, an isolated or occasional finding of apparent non-patency may occur and this, equally in anæsthetized and non-anæsthetized subjects, and (2) the result of a single insufflation, with or without anæsthesia, showing apparent non-patency, cannot be depended upon. This latter conclusion receives further consideration when the results of insufflation are compared with (1) hysterosalpingography, and (2) the incidence of pregnancy. In a series of 60 cases subsequent examination by lipiodol showed that insufflation had erroneously indicated blockage in 6. Among 115 patients who became pregnant 29 had been diagnosed as having non-patent tubes as a result of a single insufflation.

It would follow therefore that in all reported series, except where two or more insufflations (and/or a hysterosalpingogram) established non-patency, dependency on a single finding of non-patency has given too high an incidence in the past. It has been suggested that a finding of patency subsequent to one of non-patency may be explained by the therapeutic effect of the first test. This view finds no substantiation in our results since if non-patency were found on two or more occasions, no success in restoring patency was achieved by repeated insufflation.

These findings prompted investigation into the question—what prevents the gas from passing through the tubes on one occasion while it passes freely on other occasions? This problem was studied from three aspects: (1) the effect of anæsthesia; (2) the time-relationship of insufflation to the phase of the cycle (particularly the premenstruum); and (3) the rate of flow of the gas.

It seemed possible that anæsthesia might have the effect of permitting gas to pass through tubes which had shown non-patency without it, or vice versa. But this possibility received no support from the findings already mentioned, in which, of the series of patients, a false finding of non-patency was obtained in 12 cases under anæsthesia and 13 without it. Nevertheless, a small group of cases (6) was investigated to note the effect of anæsthesia on tubal patency and on apparent blockage as recorded by kymographic insufflation. Various anæsthetics were employed, viz. gas and oxygen, ether, chloroform, and intravenous evipan sodium. In 3 of the cases, insufflation was performed first *without* and immediately thereafter *with* anæsthesia; in the other 3 it was done first under anæsthesia and soon after the anæsthetic had been discontinued. No anæsthetic had any material effect on the type of tracing obtained.

(2) It is well known that, for various reasons, insufflation should not be performed during the premenstrual phase of the cycle. The hypothetical consideration that the temporary thickening of the endometrium around the uterine end of the fallopian tube may give an erroneous finding of blockage, has not been confirmed in this series of 9 cases showing normal tubal patency, when insufflated on six or more occasions at different phases of the cycle. Again, a study of the group of 25 patients with patent tubes but who showed on one insufflation apparent non-patency revealed that the latter findings occurred irregularly in the cycle and were not related to any particular phase. Corroborative information was obtained as the result of other studies: (a) Kymographic insufflation was performed on 20 consecutive days (no menstruation intervening). No material change in the type of tracing occurred at any time, all showed patency. (b) In the course of investigations, 4 further cases were encountered in which a finding of patency was followed by one of non-patency on a subsequent date. Only in 1 case was the "non-patency" finding at the pre-menstrual phase, in all the other instances insufflation had been performed in the first half of the cycle. It may be concluded that a fallacious finding of non-patency may be obtained at any point of the cycle.

(3) Numerous experimental insufflations were carried out in both anæsthetized and non-anæsthetized patients to determine whether variations in the rate of flow of gas into patent tubes could materially alter the appearance of a kymographic tracing, even to the extent of simulating tubal blockage. Numerous variations from 30 c.c. per minute to 120 c.c. per minute (the latter rate is never used in clinical routine) were employed and in varying sequences. In a few instances the excessive rate of flow of the gas caused the pressure to rise considerably, but never above 150 mm.Hg; in no case was the tracing of non-patency obtained. The phase of the cycle appeared to bear no influence on the production of tubal spasm.

To sum up, these investigations have had a negative result in that no light has been

sufflated, 29 showed tubal blockage, an incidence of 83%. This extremely high incidence of occlusion suggested the possibility of an unsuspected subclinical tuberculous salpingitis as the source of reinfection of the endometrium, and this conception in turn led me to re-consider the possible ætiology of tubal occlusion from a new angle.

IV. *An Inquiry into the Causation of Tubal Occlusion*

There is, of course, no need to discuss tubal occlusion arising from gross tubal damage. The problem under consideration at the moment is the ætiology of blockage in tubes which appear normal on bimanual examination. In the past, it has been widely accepted that in most instances the occlusion of the lumen results from gonococcal salpingitis, or from tubal infection from a nearby pelvic lesion (particularly appendicitis), or from con-genital hypoplasia. The recent finding that endometrial tuberculosis is unexpectedly common (5%) in sterile women suggested the possibility that tubal tuberculosis of a degree insufficient to be grossly recognizable, except on laparotomy, might be responsible for a much greater number of cases of tubal non-patency than is generally recognized, and led me to undertake certain investigations which I shall now discuss.

(1) *Gonococcal salpingitis as a cause of tubal occlusion.*—There is very little positive proof that, apart from gross tubal damage, gonococcal salpingitis is a common cause of tubal occlusion. It is unusual to obtain a history of any acute pelvic illness in a series of sterile women and, more important still, there is little direct evidence that the infection ever reaches the tubes in more than a very small percentage of cases of gonorrhœa. There are few published data on this point, but with the co-operation of the Public Health Department of Glasgow I have been able to obtain the following figures which, I think, are of considerable significance. The records of acute gonorrhœa in women who attended the principal clinic from 1930 to 1937 were surveyed, with special reference to the inci-dence of pelvic involvement. There were only 5 cases of the latter in a total of 540 patients. A follow-up of the 5 cases revealed that 1 subsequently had three pregnancies, but that the others had not become pregnant. During the years 1938 to 1942 (inclusive) the total number of new cases of acute and chronic gonorrhœa in females over 15 years of age, attending the principal Glasgow municipal centre, amounted to 987. Of these, there were 26 cases of acute pelvic involvement, i.e. 2·6%. In 775 consecutive cases of acute gonorrhœa, during the same period, there were 10 cases of salpingitis, i.e. 1·3%. Very careful observations have been made on this point since June 1941. Since that date a total of 979 cases have been treated, of which only 8 have developed an acute febrile pelvic lesion (less than 1%).

Even if it is admitted that a number of mild pelvic infections may have occurred, the general conclusion appears to be that the gonococcus is seldom responsible for the occlu-sion of tubes which are not palpably thickened.

(2) *Congenital hypoplasia as a cause of tubal occlusion.*—The significance of this factor was first described and stressed by Clauberg, who maintained that, in cases of infantile uterus, the tubes often share in the developmental deficiency and are consequently im-permeable. There has been a vague general acceptance of Clauberg's theory, but I am not satisfied that it is correct. The following arguments may be raised against it: (1) Clauberg's evidence was almost entirely radiological (apart from investigations on lower animals); (2) a large number of cases of uterine hypoplasia have shown normal tubal patency and function on kymographic insufflation; (3) radiographs frequently show patency in tubes presenting the long, thin, tortuous features of the "congenital hypoplastic" type; (4) in a small series of cases showing *definite* tubal blockage and treated by Clauberg's method with œstrogenic hormone none showed patency after treatment as claimed by him; and (5) tubal blockage associated with uterine hypoplasia need not be due to tubal hypoplasia but may be due to other causes, e.g. subclinical tuberculosis, as will be dis-cussed later. It is not disputed, of course, that follicular hormone produces proliferation of the mucous membrane and general hyperæmia of the fallopian tubes, as Clauberg has shown, but the point at issue is whether the hypoplastic or infantile tube is essentially a non-patent structure or not. I have approached this question from three angles: (A) a histological study of the prepubertal tube; (B) insufflation of the tubes of the fœtus and infant; and (C) kymographic insufflation in an unselected, consecutive series of un-married women.

A. *The prepubertal tube*: Fallopian tubes were removed post mortem and sectioned from cases of the following ages: (a) a 7 months' fœtus; (b) a fœtus stillborn at term; (c) a child aged 2 days; (d) a child aged 10 weeks; (e) 3 months; (f) 4½ months; (g) 7 months; (h) 16 months; (i) 3 years; (j) 4 years; (k) 8 years; and (l) 10 years. Sections were cut through fimbrial, ampullary and isthmial portions. The appearances of the tubes throughout the

All but one of the cases in my series are incorporated in his paper and it is not intended therefore to discuss the pathological aspects here.

The points I wish to discuss are:

(a) The high incidence of endometrial tuberculosis in sterility.
(b) The evidence that this estimated incidence is minimal.
(c) The duration of the disease.
(d) The effect of curettage.
(e) The results of search for tuberculous history and other tuberculous lesions.
(f) The relationship of endometrial tuberculosis to tubal occlusion.

(a) *The high incidence of endometrial tuberculosis in sterility.*—Sutherland has reported the finding of tuberculosis in 100 endometria in a consecutive series of 7,670 (including sterility cases) giving an incidence of 1·3%. It has already been pointed out that my series of 840 endometria shows an incidence of 5% tuberculosis. Further analysis shows that endometrial tuberculosis is fifteen times more common in sterile women than in those who are not.

(b) *The evidence that this estimated incidence is minimal.*—In 17 of these patients biopsy was performed more than once: when performed twice it was tubercle positive on both occasions in 5 patients, and once positive and once negative in 2 cases: when performed either three or four times in the remaining patients, on 19 occasions it was tubercle positive and on 17 tubercle negative. Obviously therefore in many instances no evidence of the disease was found on single occasions. This occasional absence of evidence prompted further study of the endometria concerned. The paraffin blocks were re-imbedded and re-orientated so that further sections might be taken from the other end of the biopsy material. This was done in twelve blocks from 6 patients. Numerous sections were examined, but there was no evidence of tuberculosis in any of them. Further light in this connexion was thrown by the examination of additional sections of the definitely positive biopsies: in several of the cases, sections showed no evidence of tubercle follicles. Moreover, in several cases in which biopsy material was divided, negative histological findings and positive guinea-pig inoculation results were obtained. It may be concluded, therefore, that absence of signs of tubercular endometritis in any given biopsy is not evidence that the disease is present and that the incidence figure of 5% in my series is an absolutely minimal one.

(c) *The duration of the disease.*—Endometrial tuberculosis was found to be still in evidence after the following lengthy periods of time in 6 patients: (1) two and a half years: (2) five years; (3) two and a third years; (4) two years; (5) two and a half years; (6) seven and a half years. Follow-up also showed that not one sterility patient, with endometrial tuberculosis, became pregnant.

(d) *The effect of curettage.*—Although it was considered most improbable that even very thorough curettage of a tubercular endometrium would "cure" the condition, studies were carried out to observe the recurrence of the tubercle follicle and to determine its time-interval. Four sterile patients were investigated.

The findings may be summarized: Tubercular endometritis was found to have recurred at the following intervals of time after thorough curettage under anæsthesia: (1) thirty-four days; (2) twenty days; (3) three months; and (4) twenty-seven days. There seems little doubt therefore that reinfection of the endometrium rapidly recurs after curettage. The question naturally arises as to the location of the focus from which reinfection occurs. Investigating this matter, careful inquiry was made to the previous history of the patient and a detailed search for tubercular lesions in other organs of the body was carried out.

(e) *The results of search for tuberculous history and other tuberculous lesions.*—In none of these cases was pelvic tuberculosis diagnosed or suspected when endometrial biopsy was performed. All were noted as enjoying good health and, with the exception of three cases, there was no history suggestive of tuberculosis in childhood, or adolescence; the three exceptions were: (1) Case No. 452, aged 28, "pleurisy and gastro-enteritis" at age of 17; (2) Case No. 454, aged 29, "T.B. gland of neck" at age of 5; and (3) Case No. 76, aged 24, "tabes mesenterica" at age of 14 (nine months in sanatorium). Radiographs of the chest in 10 cases showed no evidence of pulmonary tuberculosis in 7, but 2 showed apical tuberculosis of both lungs (Case No. 21 and Case No. 469) and the other calcified plaques at both apices (Case No. 98)—in the latter, radiograph of the spine showed Pott's disease; no calcified glands were seen in abdominal radiographs (4 cases) or in pelvic ones (4 cases).

(f) *The relationship of endometrial tuberculosis to tubal occlusion.*—I have left to the last the consideration of the incidence of tubal occlusion in cases of endometrial tuberculosis: in 18 of the 20 cases tubal insufflation was performed, and showed non-patency in 14 (78%). In the second series of 22 cases, insufflation was performed in 17 and showed non-patency in 15 (88%). Combining the two series, it will be seen that out of 35 cases in-

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*October* 21, 1943]

Circumscribed Scleroderma of the Buccal Mucous Membrane.—H. W. BARBER, M.B.

Mr. J. P. K. W., aged 43, consulted me September 6, 1943, for a white patch on the mucous membrane of the left side of the lower lip. It had been noticed for the first time some six months previously, and for a while increased in size.

On examination there was seen at the above site a sharply circumscribed patch, white in colour, and extending downwards from the margin of the vermilion border of the lip to the alveolar sulcus. The patch was indurated, as could be determined by pinching up the affected portion of the lip between the thumb and forefinger. It was narrow above, broadening out towards the lower part, and resembling somewhat in shape a primitive stone-hammer. Its configuration recalled the band form of scleroderma sometimes seen on the forehead and scalp—*en coup de sabre.* An important point is that the patch was depressed below the level of the surrounding normal mucous membrane. This prevents confusion with leucoplakia.

As regards the causation of the condition in this case, I think it may be of significance that at the time of its appearance the patient was passing through a period of great strain owing to the serious illness of his mother and her subsequent death, apparently from shock after an air raid.

Scleroderma of the mucous membranes is extremely rare, and even authoritative accounts of the disease often omit to mention it. In Anderson's classical case of scleroderma involving the areas of skin supplied by all three divisions of the Vth nerve the mucous membranes were also involved (Anderson, W., *Brit. J. Derm.*, 1898, 10, 46).

There is now considerably less induration of the patch and in places it appears that spontaneous resolution is occurring.

The President: I have had a case of morphœa on the back clear up completely in eight months from its first appearance.

Dr. F. Parkes Weber: I would compare this mucosal sclerodermatous patch on one side of the frenum linguæ to the ivory-like sclerodermatous line occasionally seen running from the root of the nose upwards on one side of the middle line of the forehead. The consistency in such cases is very hard, and the appearance of ivory is striking. I cannot believe that such patches can clear up completely. It seems to me that there must be hardly any blood-vessels in these patches, so that troublesome chronic ischæmic ulceration is very likely to occur.

The President: I should be glad to hear the experience of members as to whether it is a common thing for morphœa to ulcerate. I have a patient, a woman aged 38, now in St. Bartholomew's who is covered with ivory-like patches of morphœa nearly every one of which is ulcerated deeply in the centre.

Dr. S. R. Brunauer: This case is very interesting. When I was writing the chapter "Scleroderma" for Jadassohn's handbook, I could find only a very few cases in the literature of circumscribed scleroderma of the mucous membrane. Dr. Barber's case, therefore, is all the more remarkable, because it recalls the scleroderma *en coup de sabre* of the forehead.

Dr. Barber: Patches of morphœa on the skin frequently disappear spontaneously and completely, leaving a brownish stain for a time.

As regards ulceration in the patches, I had a patient with a single large patch on one leg, the central part of which was ulcerated, but rather to my surprise this healed under simple treatment.

Pemphigus Foliaceus.—J. E. M. WIGLEY, M.B.

F. C., male, aged 32.

Eighteen months' history. Eruption first appeared on the chest, back, face, neck, and ears. Seen by Dr. Goldsmith in January 1943, when a diagnosis of "low-grade impetigo implanted on seborrhœic dermatitis" was made.

I saw him first on July 2, when an eruption was present on the face, about the ears, the chest, the back and the limbs. There were varying sized pigmented areas with circinate and gyrate erythematous macules, some irregular crusted lesions, and one or two small bullæ. He complained of slight irritation, but said that his skin was sore in many places.

When seen again on August 6 the eruption was more of a herpetiform nature and the irritation was more marked. A diagnosis of dermatitis herpetiformis was made, and he was admitted to hospital.

series are those of a patent structure and there is no evidence that canalization of the Mullerian ducts is often (if ever) incomplete.

B. *Insufflation of the tubes of the fœtus and infant*: The material studied was obtained post mortem from a series of stillborn infants and neonatal deaths in the Glasgow Royal Maternity Hospital and from fatal cases in the Royal Hospital for Sick Children, Glasgow. The examination was carried out as soon as practicable after death, usually within a few hours. 12 cases were insufflated. All showed tubal patency:

Age	Number	Age	Number
5-months' fœtus	... 1	10 days 1	
Stillborn 1		11 days 1	
4 days 1		19 days 1	
6 days 2		2 months 1	
7 days 1		4 years 1	
8 days 1			

(Skiagrams demonstrating tubal patency in two infants were shown.)

C. *Insufflation in unmarried women*: No woman was admitted to hospital and subjected to this test simply for purposes of experiment. All of the patients thus examined had been admitted for the treatment of some definite complaint, the commonest being dysmenorrhœa. The opportunity was taken at the time of operation to apply this test. 100 have been studied to date, their ages ranging from 13 to 39 years. It was estimated that in over one-third of the patients the uterus appeared to be of the small, hypoplastic type.

Insufflation showed that in all cases the tubes were permeable to gas. In 93 of them the gas passed at low pressure, but in 7 a certain degree of spasm appeared to be present, as evidenced by the fact that gas reached a high pressure before passing.

In conclusion it may be stated that the evidence obtained from these three separate lines of inquiry suggests that impermeability of the tubes is seldom a congenital defect.

(3) *Subclinical tuberculous salpingitis as a cause of tubal occlusion.*—It will be remembered that, in the course of this investigation, unsuspected subclinical endometrial tuberculosis was found in a relatively high percentage (5%) of sterile women. Now, since endometrial tuberculosis in general is almost invariably secondary to tuberculous infection of the tube, it is highly probable that subclinical tubal tuberculosis is present in at least 5% of sterile women. Further, it is well known that endometrium often escapes infection even when the tubes are the seat of gross tuberculous lesions, and it is, therefore, highly probable that in sterile women the incidence of subclinical tubal tuberculosis is much higher than 5%. This suggests the possibility that subclinical tuberculosis of the tube may be the cause of occlusion in a tube which appears normal to palpation. An endeavour was made to obtain positive evidence on this point, and two separate methods of investigation were utilized. First, the incidence of tubal occlusion in cases of endometrial tuberculosis was investigated and, second, histological proof of tuberculous infection was looked for in tubes which had been found to be blocked.

The incidence of tubal blockage in endometrial tuberculosis was found to be 29 in 35 cases, i.e. 83%. This compares with an incidence of 38% over the total series of 500 sterile women, including those in whom endometrial tuberculosis was present.

The second line of evidence was more difficult to apply, because only a small number of women were willing that an attempt should be made to restore patency of the tube by operation. So far I have had an opportunity of studying the histology of three such tubes, a small piece being removed in the course of salpingostomy. The series is too small from which to dogmatize, but nevertheless it is striking that all three specimens showed tuberculous infection.

In view of these findings I feel justified in putting forward the view that tubal blockage may, in a considerable number of cases, at any rate, be due to a subclinical tuberculous salpingitis.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*October* 21, 1943]

Circumscribed Scleroderma of the Buccal Mucous Membrane.—H. W. BARBER, M.B.

Mr. J. P. K. W., aged 43, consulted me September 6, 1943, for a white patch on the mucous membrane of the left side of the lower lip. It had been noticed for the first time some six months previously, and for a while increased in size.

On examination there was seen at the above site a sharply circumscribed patch, white in colour, and extending downwards from the margin of the vermilion border of the lip to the alveolar sulcus. The patch was indurated, as could be determined by pinching up the affected portion of the lip between the thumb and forefinger. It was narrow above, broadening out towards the lower part, and resembling somewhat in shape a primitive stone-hammer. Its configuration recalled the band form of sclero-derma sometimes seen on the forehead and scalp—*en coup de sabre*. An important point is that the patch was depressed below the level of the surrounding normal mucous membrane. This prevents confusion with leucoplakia.

As regards the causation of the condition in this case, I think it may be of signifi-cance that at the time of its appearance the patient was passing through a period of great strain owing to the serious illness of his mother and her subsequent death, apparently from shock after an air raid.

Scleroderma of the mucous membranes is extremely rare, and even authoritative accounts of the disease often omit to mention it. In Anderson's classical case of sclero-derma involving the areas of skin supplied by all three divisions of the Vth nerve the mucous membranes were also involved (Anderson, W., *Brit. J. Derm.*, 1898, 10, 46).

There is now considerably less induration of the patch and in places it appears that spontaneous resolution is occurring.

The President: I have had a case of morphœa on the back clear up completely in eight months from its first appearance.

Dr. F. Parkes Weber: I would compare this mucosal sclerodermatous patch on one side of the frenum linguæ to the ivory-like sclerodermatous line occasionally seen running from the root of the nose upwards on one side of the middle line of the forehead. The consistency in such cases is very hard, and the appearance of ivory is striking. I cannot believe that such patches can clear up completely. It seems to me that there must be hardly any blood-vessels in these patches, so that troublesome chronic ischæmic ulcer-ation is very likely to occur.

The President: I should be glad to hear the experience of members as to whether it is a common thing for morphœa to ulcerate. I have a patient, a woman aged 38, now in St. Bartholomew's who is covered with ivory-like patches of morphœa nearly every one of which is ulcerated deeply in the centre.

Dr. S. R. Brunauer: This case is very interesting. When I was writing the chapter "Scleroderma" for Jadassohn's handbook, I could find only a very few cases in the literature of circumscribed scleroderma of the mucous membrane. Dr. Barber's case, therefore, is all the more remarkable, because it recalls the scleroderma *en coup de sabre* of the forehead.

Dr. Barber: Patches of morphœa on the skin frequently disappear spontaneously and completely, leaving a brownish stain for a time.

As regards ulceration in the patches, I had a patient with a single large patch on one leg, the central part of which was ulcerated, but rather to my surprise this healed under simple treatment.

Pemphigus Foliaceus.—J. E. M. WIGLEY, M.B.

F. C., male, aged 32.

Eighteen months' history. Eruption first appeared on the chest, back, face, neck, and ears. Seen by Dr. Goldsmith in January 1943, when a diagnosis of "low-grade impetigo implanted on seborrhœic dermatitis" was made.

I saw him first on July 2, when an eruption was present on the face, about the ears, the chest, the back and the limbs. There were varying sized pigmented areas with circinate and gyrate erythematous macules, some irregular crusted lesions, and one or two small bullæ. He complained of slight irritation, but said that his skin was sore in many places.

When seen again on August 6 the eruption was more of a herpetiform nature and the irritation was more marked. A diagnosis of dermatitis herpetiformis was made, and he was admitted to hospital.

A blood-count was within normal limits (eosinophils 1%).

Examination of the blister fluid did not reveal an eosinophilia. He was treated with liq. arsenicalis but showed intolerance when a dose of m̨ viii t.d.s. was reached. He was discharged on August 28, 1943, with the rash more or less unaltered.

He then received ultraviolet irradiation and five injections of ⅓ gr. sodium cacodylate as an out-patient.

On September 29, 1943, he returned complaining that he had not had a night's sleep for a fortnight because of soreness of the skin, not because of irritation. His skin was blistering and peeling rapidly and there was a great deal of exudation from the lesions. He received a course of sulphapyridine without effect on the skin condition (51 g. over a period of fourteen days).

The patient's present condition shows an extensive eruption over the face, ears, neck, upper trunk, and limbs. Many of the lesions are flat crusts over an occasional gyrate erythematous base, but here and there definite flat blistering lesions can be seen. These are the places where the patient has noticed that the skin peels easily, and may be taken as a positive Nikolsky's sign.

I think the diagnosis of pemphigus foliaceus can be made with some confidence on the above history and clinical picture.

Dr. W. N. Goldsmith: This case reminds me of another case which I first diagnosed as seborrhœic dermatitis. He then developed blisters, and I considered the possibility of dermatitis herpetiformis. He was later seen by Dr. Barber who diagnosed the Senear-Usher syndrome. That case has undergone fluctuations, but on the whole has been getting worse. He, too, did not respond to sulphonamide. He responded for a time to gold.

Dr. Elizabeth Hunt: A comment might be made on the absence in this case of the distinctive odour usually noticed in pemphigus foliaceus.

Dr. Wigley: I am asked whether the patient had local sulphonamide before he had sulphonamide by mouth. That did not happen so far as I am aware.

The President: I have seen cases of dermatitis due to sulphathiazole in which sensitization has been produced by external application and the substance has then been given internally, with the result that a terrific dermatitis has developed. But those cases have not looked like this one shown by Dr. Wigley. The odour can be controlled by sulphanilamide 5% in zinc cream. My patient with pemphigus foliaceus had this for two years without becoming sensitized to it.

Mycosis Fungoides.—THERESA KINDLER, M.D. (for J. E. M. WIGLEY, M.B.).

A. W., male, aged 71, has had a very irritating rash for about six months which first appeared after a course of myocrisin injections, given for arthritis. He has lost 2 st. in weight since the complaint started. When I first saw him four months ago, the rash consisted of circinate red, purplish and reddish-brown, slightly scaling patches of various sizes. Distribution chiefly over chest, sides of trunk and limbs. Later on many coalesced to polycyclic figures, which became infiltrated in the axillæ, groins, at the inside of the thighs and in the natal cleft. Fresh plaques appeared from time to time; others involuted, some spontaneously, some apparently as the result of X-ray treatment, the newest lesions being erythematous patches. In the last month several wartlike growths developed on the infiltrated areas of the thighs. The mucosæ are free, except for a leucoplakia on the right cheek at the interdental line. Moderate inguinal and cervical adenitis. The Wassermann and Kahn reactions are negative. The blood-count was normal, except for the high percentage of monocytes which from 8% in July increased to 27% in September; eosinophils were only 1%.

Biopsy (Dr. M. Loewenberg): The histological picture from a fresh lesion is indefinite; but another one from an infiltrated area shows a very massive polymorphous infiltration of the papillary and subpapillary layers situated in a loose network of connective tissue bundles. There are lymphocytes, epithelioid cells, eosinophils, mast cells, cells with pseudopodia, and occasional giant cells with two to three nuclei. Between these cells are numerous fragments of broken-down protoplasm and nuclei. The elastic tissue, sebaceous and sweat glands are missing in the infiltrated areas. In the lower cutis the elastic fibres consist of coarse, broken fragments; sweat glands are well preserved here. The connective tissue has hardly suffered at all. In the epithelium there is acanthosis and spongiosis. In some places there is an upward immigration of cells in the epidermis and the borderline between the epidermis and cutis has disappeared.

The histological picture together with the clinical one, the colour, outline, infiltration and erratic course of the eruption, and the disappearance and reappearance of the lesions suggest the diagnosis mycosis fungoides. Also the high percentage of monocytes is frequently observed in this disease; figures up to 60% have been recorded. There is no eosinophilia here.

Dr. Robert Klaber: Whatever the eruption on the body may be the lesions on the right side of the mouth are typical of lichen planus.

Dr. W. Freudenthal: One of the two biopsies would do for a lichen planus as well as for a mycosis fungoides, but the other is in favour of a mycosis fungoides, although a drug eruption cannot be excluded.

The President: One can certainly get a great amount of hyperkeratosis in gold dermatitis, but the fact that the lesions are still progressing seems against the theory of gold eruption.

Dr. Wigley: I have been able to see this case on several occasions. At first, I thought it could be a drug eruption, e.g. phenolphthalein, but there was no history to support this. It is a very long time for the gold injections, given in January, to be still producing lesions. At no time have I seen lesions which I regarded as lichen planus. I think that the histology is very suggestive of mycosis fungoides.

Dr. C. H. Whittle: What struck me is the atrophy which is noticeable in some of the lesions on the lower part of the trunk. The case is of great interest if it turns out to be mycosis fungoides with atrophy.

Dr. Kindler: At no time was there any primary lesion resembling that of lichen planus. We will watch the case and report about it further to the Section.

Erythema Annulare Centrifugum (Darier).—C. H. Whittle, M.D.

J. H. I., aged 36, a radio electrician.

Three months' eruption on the right side of the neck of red rings, irritable, spreading centrifugally, leaving normal skin in their wake.

Previous history of multiple tuberculous glands, right side of neck at age of 14, removed by excision and leaving extensive scars. There is an arabesque made up of four arcs of circles, the largest 6 cm. diameter, lines of bluish red raised papules, only in places slightly scaly, and about 6 mm. diameter. An early commencing ring on the chest 1 cm. diameter from which biopsy was taken. The friction and pressure of the collar appear to make the lesions redder and more raised.

Scales were examined for fungus.

Biopsy (shown): Some increase in prickle-cell layer, some hyperkeratosis, œdema and moderate infiltration of the corium with round cells, polymorphs, and two microabscesses in the epidermis beneath the horny layer.

Treatment and course.—Tar and Whitfield's ointment resulted in temporary improvement only.

Mantoux reaction very strong positive to 0·1 c.c. 1:1,000 human and bovine tuberculins with wheals 4 to 5 in. across and vesication. Some general malaise resulted and the reaction persisted for several days.

Wassermann reaction negative.

On the second examination for fungus after a long hunt, a single but definite length of branching mycelium was found. I cannot find any evidence of fungus infection elsewhere in the body. Sutton ("Diseases of the Skin", 1939, 10th ed., Vol. I, p. 150) mentions the association of erythema centrifugum of the Darier type in at least three cases with epidermophytosis in another part of the body: the erythema disappeared when the fungus infection was cured.

A veterinary examination of the patient's dog showed no parasitic or fungus infection.

Pigmented Lesion of Neck.—G. B. Dowling, M.D.

The patient is a woman aged 35, who three and a half years ago developed an oval, red patch on the left side of the neck. It has grown a little subsequently, but has not changed in appearance during the last year or more. There has been a moderate degree of itching.

An oval, sharply marginated, pigmented area on the left side of the neck; in colour a mottled brown; slightly infiltrated; does not appear to be atrophic. The pigmentation is disposed in small striæ, the background appears to be faintly red. Small lichenoid papules are to be seen in the area, the surface of which, as a whole, is slightly rough.

Dr. F. Parkes Weber: I should like to suggest the possibility of something in the nature of a "delayed" nævoid patch. It is not certain that it only started three and a half years ago.

The President: Was there not some atrophy between the papules?

Dr. Dowling: I thought not—I looked very carefully.

The President: Do you think a section would settle that question?

Dr. F. Parkes Weber: Not absolutely. Such nævoid patches on the skin may in microscopic structure imitate dysplastic diseases.

Dr. C. H. Whittle: I thought it was a nævoid condition which the patient had scratched, causing lichenification.

Dr. Dowling: It was red, pigmented and irritable from the beginning. A pigmented nævus is not irritable as a rule.

Folliculitis Decalvans in Mother and (?) in Child.—W. N. GOLDSMITH, M.D.

G. N., woman, aged 20.

Present condition (October 19, 1943).—Most of the top of the scalp is bald. The skin appears slightly crinkled but not obviously atrophic. At the occiput, where the hair is still present, there are irregular patches of redness centring around the hair roots at some of which there are little scales or scabs. A large proportion of the hairs issuing from the inflamed follicles are broken off short. There are no pustules and the stumps when pulled out are quite dry.

History.—She states that this trouble started at the age of 4 years. She has never had any skin disorder elsewhere. I first saw her at the West Herts Hospital on September 21, 1943, when the occiput was more scaly. I prescribed.

| Hydrarg. ammon. | ... | ... | ... | ... | gr. 20 |
| Ung. aquos. | ... | ... | ... | ... | ... | ʒ 1 |

which reduced the scaling and scabbing but not the degree of redness. Stumps examined in KOH revealed no fungus. Cultures are being made.

Her daughter, V. N., aged 2 years, has also been noticed by the mother for some little while to have similar sores on the scalp. When I first saw her on September 21 there were little crusted spots difficult to distinguish from impetigo. After treatment with the mercurial ointment the crusts have gone and there remain streaks of reddened follicular orifices across the top of the scalp very like those of the mother, and in an arrangement unlike impetigo. There is, however, so far no baldness or breaking of the hair.

Comment.—The interest of these cases is in the involvement of mother and daughter and in the early onset. I have not found any evidence of keratosis pilaris or ichthyosis.

Dr. G. B. Dowling: This may possibly be a case of favus. I presented to the Section a case of favus of the scalp some years ago (*Proc. R. Soc. Med.*, 1932, 25, 1550). The patient was a young girl who had been for many years suffering from a gradually increasing cicatricial alopecia. The diagnosis was made of folliculitis decalvans, but after several weeks I noticed that small scabs were developing here and there. These contained a feltwork of mycelium which was shown by culture to be favus. The girl had spent most of her life in Istanbul.

POSTSCRIPT (31.12.43).—Dr. Dowling was right. Cultures from stumps taken before the cases were demonstrated, as well as some more taken since, have all grown *Achorion schœnleinii* (Dr. A. C. Cunliffe). Some of these latter stumps when withdrawn brought with them a tiny bead of pus. The patients were sent for X-ray epilation to Ashridge Hospital where Dr. Wigley found that numerous affected hairs gave the characteristic fluorescence under Wood's light. Fungus was also seen in the stumps. Nothing remotely resembling scutula was present. It is also unusual for the hairs to break off short. The patients have not been abroad.   W. N. G.

? Poikiloderma (Civatte).—GEOFFREY DUCKWORTH, M.R.C.P.

Mrs. H., aged 47. For eight months has noticed a blackish pigmentation and redness that began about the upper eyelids and cheeks and which has spread over the bridge of the nose, and downwards, to the chin and front of the neck. The skin used to be conspicuously greasy, but is now remarkably dry.

On examination there is a macular and reticulate dark brownish pigmentation on a reddish ground of skin, which seems a little thickened. There is no obvious atrophy, but the dryness suggests at least a functional inactivity of the glands of the skin.

The last menstrual period was in July, and the one before that a year earlier. Previously they had always been regular since the birth of a daughter, now 26 years of age. She thinks the pigmentation was less marked at the time of the last period. The health otherwise is good, and nothing abnormal has been discovered apart from a little dandruff and some gingivitis. There is no history of applications of tar or oil, locally, and none of the ingestion of liquid paraffin or excess of fats. Her father was a Sicilian, her mother a fair-haired Englishwoman. Her complexion is olive.

It may be interesting to see if stilbœstrol has any helpful effect, in view of her impression that the disfigurement was less obvious during the time of the last period.

Dr. F. Parkes Weber: The only diagnosis I can think of, apart from the tentative one which Dr. Duckworth has given, is that the case might be a premature geroderma, that is to say, a premature senile condition of the skin of the face connected with the practically complete cessation of menstruation. With regard to doing anything I do not know whether what I have suggested opens up the question of trying any hormone treatment.

[Other cases shown at this meeting will be published in the next issue of the *Proceedings* of the Section of Dermatology.]

Section of Urology

President—E. W. RICHES, M.C., M.S.

[*October* 28, 1943]

Paralysis of the Bladder

[*Abridged*]

PRESIDENT'S ADDRESS

By E. W. RICHES, M.C., M.S.

The Mechanism of Micturition

THE theory of sympathetic and parasympathetic antagonism fails to provide a satisfactory explanation of the peripheral mechanism of micturition. There is no separately innervated sphincter at the internal vesical orifice; the muscle here forms part of the detrusor musculature and is supplied by the parasympathetic nerves. Contraction of the longitudinal fibres of the detrusor pulls the bladder neck open mechanically whilst the circular fibres exert pressure on the contents. Interruption of the parasympathetic nerves causes paralysis of the whole bladder with relaxation at the internal orifice. The striated external sphincter and perineal muscles complete the continuity of the vesical and urethral musculature. The segmental origin of the parasympathetics (S. 2, 3, and possibly 4) to the detrusor, and of the somatic supply (S. 3 and 4) to the external sphincter make up the sacral "centre" for micturition. Cerebral control is inhibitory to the para-sympathetic-detrusor mechanism, and its removal by transection of the cord allows the stretch reflex to act unhindered.

The trigone, innervated by the sympathetic, is *not* essential for normal micturition (Langworthy, Kolb and Lewis, 1940) and is concerned with the sexual function (Macalpine, 1934).

This account is based on a study of 30 cases of bladder paralysis seen in routine practice and 35 war injuries of the spine seen in the special centres and reported else-where (Riches, 1943b).

Methods of Study

The special urological methods used are cystoscopy, cystography and cystometry.

Cystoscopy shows alteration in size from atony, or hypertrophy at a later stage, fine trabeculation, and relaxation of the bladder neck giving a funnel-shaped deformity (Barrington, 1915; Burns, 1917). The funnel neck is an almost constant occurrence and was present in 23 out of 25 cases cystoscoped, the other 2 being females. Its degree usually depends on the amount of bladder distension, but it may become fixed and very wide in a contracted bladder. It can be simulated after endoscopic resection of the prostate, or in lateral lobe enlargement, and it can be produced temporarily by a spinal anæsthetic. It is the most important sign of bladder paralysis, but it must be looked for deliberately if it is not to be missed.

Cystography.—An atonic paralysed bladder is often bilocular; if the bladder has been allowed to become contracted there may be a ureteric reflux, but this is not seen in the atonic stage and is not the route of early ascending infection. Peri-ureteral lymphatics form the more probable route.

Cystometry is of some value as a record of the type of bladder under observation, and as a check on progress. A modification of the existing appliances has been described as the "Double Y" tidal irrigator and cystometer (Riches, 1943a) and is convenient for clinical use.

CLINICAL MATERIAL

Of the 30 cases studied 13 have had spina bifida occulta, 5 were tabetics, 2 had cord lesions, 6 cauda equina lesions, 2 had disseminated sclerosis and in only 2 where signs of bladder paralysis were present was it impossible to find a neurogenic cause.

JAN.—UROL. 1

A. *Spinal Fusion Defects*

Although the defect may only be a mild degree of spina bifida occulta the constant accompaniment of the typical cystoscopic picture leaves no doubt that the urinary symptoms are produced by it.

CASE I.—*Enuresis:* A boy of 14 with lifelong nocturnal enuresis of such degree that he he could not be kept at a public school. Cystoscopy under a general anæsthetic showed

FIG. 1 (*Case II*).—Sacral spina bifida occulta.

FIG. 2 (*Case II*).—Spina bifida occulta. Cystogram.
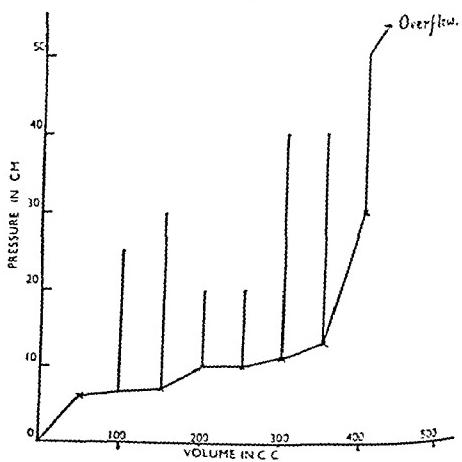
FIG. 3.—Cystometrogram of Case II. 5.12.42.

a clean bladder of 8 oz. capacity and a complete funnel-neck deformity visible at every degree of distension. X-ray showed failure of fusion of the first and second sacral laminæ. He was referred for examination prior to proposed psychological treatment; it is not likely that it would have helped him.

CASE II.—*Frequency:* A man of 29 complaining for one year of hourly frequency of micturition by day and little better by night. The urine was not infected and there were no abnormal signs in the central nervous system. Cystoscopy showed a clean trabeculated bladder with a capacity of 9 oz. and a complete funnel-neck deformity. There was radiological evidence of non-fusion of the laminæ of S. 1-4 (fig. 1); the upper urinary tract was normal, blood urea 23 mg. per 100 c.c. and Wassermann reaction negative. A cystogram (fig. 2) showed the domed bladder often found with nerve lesions, and cystometry an irritable bladder with many detrusor contractions emptying at a fill of 400 c.c. and a pressure of 50 to 60 cm. (fig. 3).

One can imagine similar contractions occurring during normal bladder filling, inadequate to empty it, but enough to produce frequent urination. This type of curve probably indicates an involvement of the anterior roots.

CASE III.—*Stress incontinence:* A sailor of 41 who was blown up on convoy duty two years earlier by bombs exploding in the sea on both the port and starboard side. He was knocked flat but not hit and continued to serve his gun for three hours. On going off watch he found his trousers wet through, and thought it might be from the sea but was disillusioned later when he found that he passed urine involuntarily on any sudden strain or fright. He was invalided from the Navy and now in civilian life finds that he is incontinent at any unexpected noise like a car back-firing. He gets up two or three times in the night to pass urine but does not wet the bed. If he goes out for any length of time he wears a bag. Examination of the nervous system was negative. The urine was not infected but after passing one pint he still had a residual of half a pint. Cystoscopy showed a clean bladder with fine trabeculation and a funnel-neck deformity. An X-ray revealed a defect of the sacral laminæ, ossification being poor in the first piece and decreasing progressively from the third to the fifth neural arch, with a wider canal than normal. Cystometry showed an atonic curve with few and feeble detrusor contractions. There was some sensation of distension at 500 c.c. and thereafter the pressure rose a little more steeply but only reached 20 cm. at a fill of 700 c.c. when he felt uncomfortable.

This is the type of curve obtained when the nerve involvement is mainly of the posterior roots.

CASE IV.—*Overflow incontinence:* A man of 59 who had been operated upon for spina bifida in infancy; there was a protrusion of skin over the sacrum. After a period of increasing frequency of micturition he became incontinent and this had persisted for the past year. He had no desire to pass urine, but tried every two hours and passed a fair stream with little difficulty. The bladder was distended, the prostate not enlarged, blood urea 33 mg. per 100 c.c. and Wassermann reaction negative in blood and C.S.F. He had over a pint of residual urine which was not infected, and cystoscopy showed a finely trabeculated bladder with a funnel-neck deformity. In this case there was a patulous anal sphincter and a relative anæsthesia over the third, fourth and fifth sacral segments; X-ray showed a deficiency of the sacral laminæ. He declined suprapubic cystotomy but consented to a further exploration of the sacral swelling. The scar was excised and a band of fibrous tissue extending into the spinal canal removed; this was reported as the remains of a meningocele. Two and a half years later the incontinence was unchanged and he continued to wear a rubber urinal. Irreversible changes had been produced in the affected nerves.

These four cases give some indication of the varying types of urinary symptoms encountered in spinal fusion defects and show the transition from frequent micturition and enuresis through stress incontinence to overflow incontinence. Loss of control is commoner than acute retention although this may occur; the type of disturbance appears to depend not only on the degree of nerve injury and the relative involvement of anterior and posterior nerve roots but also on the age of the patient; in the earlier stages the phenomena are those of nerve irritation, but as growth proceeds and the nerves are further stretched or pressed upon paralytic effects supervene. Some cases have no symptoms and are only discovered on the occurrence of infection or quite by chance as in the treatment of a papilloma of the bladder. These are likely candidates for the delayed onset of symptoms after some additional strain or shock such as was seen in Case III.

Treatment.—The surgical principle of treating the cause should be followed, and more of these cases should be submitted to an exploratory operation at the site of the spinal defect at an early stage. The nerve involvement is sometimes due to pressure of a lipoma or traction by fibrous tissue and is capable of relief; even if a cure cannot be promised in all cases there is some hope of preventing the progressive damage which is otherwise likely. Successful results have been reported by Mertz and Smith (1930); Ingraham and Swan (1943) explored 26 cases in children: the commonest finding was a lipoma, either extra- or intra-dural or both, and good results were claimed in 13, or 50%. Where the main involvement is of motor fibres ephedrine or belladonna may help to check the frequency; where sensory fibres are chiefly affected drugs of the acetylcholine type should be tried. For incontinent cases gracilis muscle transplants have been advocated; for the rare cases with retention a high suprapubic catheterization is probably the best solution

and urethral catheterization should be avoided as it is the surest means of producing urinary infection.

B. *Tabes*

In tabes there is no interference with the motor side of the reflex arc, but the gradual sensory loss leads eventually to chronic overdistension with permanent loss of tone of the detrusor so that its contractions are not sufficiently strong to empty the bladder. Residual urine collects and if it becomes infected the consequences may be most serious. Tabetics are often in the prostatic age-group when first seen, but the differential diagnosis is usually obvious on cystoscopy; the two conditions may co-exist.

CASE V.—A man of 71, a tabetic, was admitted for retention with overflow; for years he had complained of difficulty of micturition, and he passed urine four or five times at night. The bladder was drained by a urethral catheter and this led to urinary infection which was not formerly present. Cystoscopy showed a large trabeculated bladder with a false diverticulum at the fundus and a funnel-neck deformity; both lateral lobes of the prostate were enlarged into the urethra. A cystogram confirmed the irregularities and showed the funnel neck. Cystometry showed an atonic bladder with no feeling of distension until its content was 700 c.c. when the pressure was still only 10 cm. On further filling there were some poorly sustained detrusor contractions, and the pressure rose to 35 cm. at 1,000 c.c. fill. There was no return of bladder function after seven weeks' treatment by catheter, and in view of the cystometric evidence of some motor activity I decided to resect the lateral prostatic lobes. He passed urine when the catheter was removed and after a month another curve was done which showed a voiding pressure at a fill of only 400 c.c. Residual urine after six weeks was only 1 oz. and eighteen months later it remained the same. He was then quite symptom-free and did not have to get up at night at all. The bladder picture was unchanged save for the absence of the lateral lobes, but its capacity was still 18 oz.

Other such cases have been reported by Emmett and Beare (1941). It is when retention develops that the treatment of the tabetic bladder becomes difficult. In the earlier stages catheterization and infection may be postponed by the use of acetylcholine derivatives.

C. *Paralysis after a Spinal Anæsthetic*

In these unfortunate cases the usual immediate sequel is retention of urine with an atonic bladder as in cauda equina lesions but later incontinence may develop if the bladder is allowed to become contracted.

CASE VI.—A man of 67 whose prostate had been resected under stovaine spinal anæsthesia one year before I saw him; he now had constant incontinence. There was anæsthesia over the second, third and fourth sacral cutaneous segments and absent anal and bulbo-cavernosus reflexes. The bladder held only 3½ oz. of infected urine and had a funnel neck; its capacity was increased by weekly lavage and distension to 9 oz. Cystography then showed a ragged outline, a wide funnel neck and a reflux up a distended left ureter. Cystometry was difficult owing to the contracted musculature but gave a steeply ascending curve with no power of adaptation and no detrusor contractions. He refused suprapubic cystotomy and was still incontinent two years after the spinal anæsthetic.

This hypertrophy of the detrusor is seen at a late stage after parasympathetic lesions and has been produced in experimental animals by Langworthy and his associates after section of preganglionic parasympathetic fibres in the sacral roots. Whatever the disadvantages of a paralysed atonic bladder they are small compared with those of a contracted one which leaks constantly. The best treatment of these unfortunate cases is probably early high suprapubic catheterization which prevents this complication and does not interfere with any recovery which may ultimately take place.

D. *Cauda Equina and Conus Lesions*

Periodic reflex micturition will follow lesions of the cauda equina and I have seen it after a proved lesion of the conus, but it takes longer to develop than does the automatic bladder of a cord lesion. The problem in treatment is to prevent either over-distension in the early stages or contraction later on, whilst guarding against ascending infection. I will mention two cases in only one of which has this problem been successfully dealt with.

CASE VII.—*Conus lesion:* A girl of 20 who was thrown out of a car and sustained a fracture dislocation of the first lumbar vertebra with paraplegia. Retention with overflow developed and suprapubic catheterization was done under local anæsthesia nearly forty-eight hours after the accident. After decompression for two days tidal drainage was instituted via the suprapubic catheter and was continued for five months. The neurological signs were those of a lesion of the conus and epiconus. Cystometry two weeks after the injury showed an atonic bladder with no detrusor contractions: the curve after

twenty weeks is also shown when there were moderate detrusor contractions but no reflex micturition (fig. 4). A cystogram at this time showed that the bladder was still somewhat atonic, but distension was felt at 300 c.c., the outline was regular and there was no ureteric reflux. Cystoscopy showed a clean mucous membrane with some trabeculation, and after the cystoscope was withdrawn she was able to pass through the urethra fluid introduced by the catheter. It is now nearly six months since the injury; there has been a mild bladder infection since the third week but she has been afebrile throughout and has had no suggestion of renal infection. Excretion urography shows an apparently normal urinary tract. Her general state has been good throughout in great contrast with the frequent toxæmic course followed by such cases. The only urethral instrumentation was the cystoscopy five months after the injury.

CASE VIII.—*Fibrous stricture of cauda equina:* A man of 39 who had suffered from a sudden urinary incontinence five years previously. He had been treated at various hospitals by dilatation and lavage during the intervening period until in 1939 he had pain in his back which came on two weeks afer a fall. His back was manipulated twice without relief and nine months later the fifth lumbar spine was excised. Following this operation he had retention of urine and incontinence of fæces. I saw him nine days later when he had been catheterized intermittently. Cystoscopy showed an infected bladder holding 21 oz. with a funnel-neck deformity. There was anæsthesia over the sacral area and a patulous anal sphincter. Neurological opinion confirmed a lesion of the lower roots of the cauda equina. Automatic tidal drainage was started but failed to control the urinary infection. He was sent to a neurosurgical centre where after thorough investi-
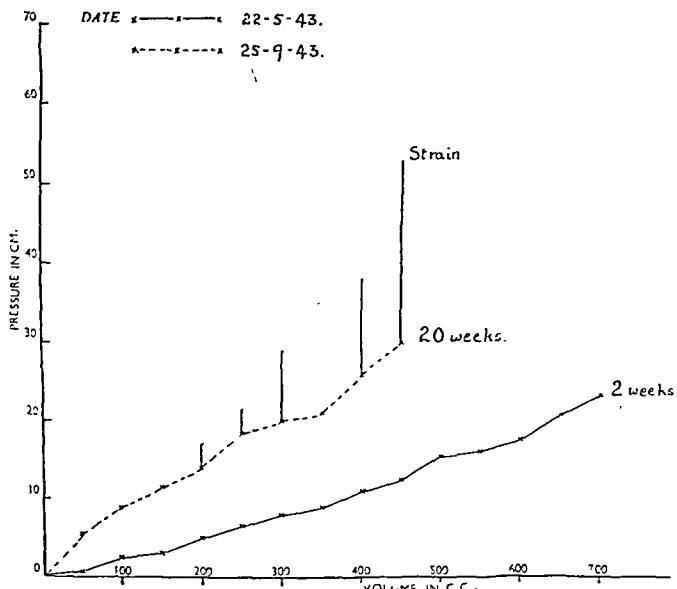
FIG. 4 (*Case VII*).—Conus lesion. Cystometrograms two weeks and twenty weeks after injury, showing the improvement in tone and return of detrusor contractions after suprapubic catheterization and tidal drainage.

gation laminectomy was performed; an extremely dense fibrous structure was found adherent to the dura and compressing the nerves of the cauda equina, and it proved impossible to separate the constrictive ring from the nerve roots. Three months later a suprapubic cystotomy was done; it was very low, the tube emerging immediately above the symphysis; it leaked, and he passed urine incontinently from the urethra. He put up with this for two years but was unable to work on account of it, and early this year I agreed to close the fistula. The bladder had now contracted down to about 2 oz. capacity (fig. 5) and showed gross cystitis, a funnel neck, and a reflux up the right ureter. The fistula was closed after two months and the bladder capacity was then increased by tidal irrigation and intermittent distension until it was 4 oz., at which point it remains ten months later. He wears an incontinence bag, but can pass a good stream by straining, leaving an ounce of residual urine. He is working and is glad that the fistula was closed. I believe that if the cystotomy had been early and high instead of late and low he would have developed a useful automatic bladder.

The periodic reflex micturition of a cauda equina lesion is subject to some control as there is a warning of distension and detrusor contractions can then be initiated by abdominal straining. In a man the resistance of the tissues around the membranous

and bulbous urethra prevents a leak unless overdistension is allowed to occur; in a woman there is more likely to be some leakage and a permanent suprapubic catheter is often of better service.

E. *Cord Lesions*

After complete supralumbar lesions periodic reflex micturition is quite automatic and uncontrollable and as the tendency towards a contracted bladder appears to be greater in these cases they are usually best served by permanent cystotomy.

CASE IX.—*Carcinoma of bronchus with spinal secondaries:* A man of 61, admitted to hospital for pneumonia; after seven weeks he complained of numbness below the umbilicus and inability to micturate properly. Catheterization gave a residual of 14 oz. and was continued thrice daily for eight days when it was replaced by an indwelling catheter to which tidal irrigation was subsequently added. He had absolute paralysis below the tenth dorsal segment; the urine was mildly infected. I saw him after a month when the bladder showed a funnel-neck deformity with a capacity of 24 oz. At a little more distension he passed a forcible stream reflexly. I did a high suprapubic catheterization and thereafter he was much more comfortable and was able to sleep through the night for the first time. Cystometry showed the hypertonic type of curve associated with cord lesions, overflow occurring at 300 c.c. fill and a pressure of 50 cm. He returned to his former hospital and died eight weeks later; autopsy showed a bronchial carcinoma with secondaries in the spine. The kidneys were free from infection and the bladder clean. The suprapubic catheter had worked perfectly throughout.

FIG. 5 (*Case VIII*).—Cauda equina lesion with low suprapubic cystotomy. Cystogram. Contracted bladder with funnel neck and ureteric reflux.

CASE X.—*Complete transverse lesion of the dorsal cord:* A soldier of 23 wounded in action in North Africa in March 1943; he received a shrapnel wound in the spine resulting in complete paraplegia below the sixth dorsal segment. He had retention of urine and was catheterized once and urine was expressed manually once. Within twenty-four hours of the injury suprapubic cystotomy was performed in a mobile neurosurgical unit; the opening was made low, immediately above the symphysis. He was evacuated by air and reached a base hospital six days after being wounded. He was pyrexial for some weeks owing to urinary infection but after a month was well enough to undergo laminectomy; a metal splinter was removed which had transected the cord at the sixth dorsal segmental level, leaving possibly a few normal fibres only. He developed a streptococcal septicæmia and multiple abscesses requiring drainage, but he was so well cared for that he survived and was evacuated to England five months after his injury. He has a very low suprapubic cystotomy which leaks sometimes (fig. 6); the bladder is contracted, holding less than 2 oz. and there is a reflux up the right ureter (fig. 7). There is a wide funnel-neck deformity with hypertrophy of the bladder mucosa; the urine is alkaline and contains gross pus; when the bladder is washed out from above the lotion comes through the urethra almost at once, and he passes urine incontinently by this route as well as by the suprapubic tube so that he must keep a bottle in the bed.

This deplorable state is due to the extreme contraction of the bladder following a very low suprapubic opening, and the condition appears beyond remedy after this lapse of time. It suggests also that the position of the opening is of even more importance than the time at which it is made.
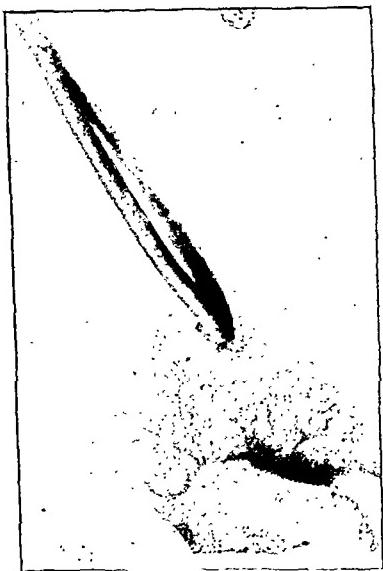
FIG. 6 (*Case X*).—Wound of dorsal cord. Low suprapubic cystotomy.

FIG. 8.—From a case of carcinoma of bronchus with spinal secondaries. Specimen sixteen days after suprapubic catheterization.

FIG. 7 (*Case X*).—Wound of dorsal cord. Cystogram. Contracted bladder (50 c.c.) with wide funnel neck and ureteric reflux. Low suprapubic cystotomy.

These cases are but a few I have chosen to illustrate how far we are from perfection in our knowledge and treatment of the paralysed bladder. We are almost unanimous in this country in condemning the urethral catheter but it is dying a lingering death, like the unfortunate patient for whom it is used. Early suprapubic cystotomy is a better

alternative at least in theory, but in practice it leads too often to a low fistula which leaks and allows the bladder to contract. This is usually due to an incision immediately above the symphysis, but even if the tube is brought out at the top of the incision the wound may give way, especially in a paralysed abdominal wall, and the final result is the same; I prefer a short transverse incision half-way up to the umbilicus. It is because of these results that I have suggested the method of suprapubic catheterization which I have described elsewhere (1943*a*). The high point of entry appears to prevent the extreme degree of bladder contraction seen in some of these cases, and the technique is simple.

(The operation was shown in a film.)

Tidal drainage is not an essential part of the treatment and it may be a danger unless everyone, down to the most junior probationer, understands what it is for. I think its main value may prove to be in the maintenance of an adequate capacity in the hypertonic bladder of high spinal lesions: overdistension is a greater danger in cauda equina lesions, but of the two evils overcontraction is the worse in its effect on the ultimate well-being of the patient. Ascending infection leading to pyelonephritis is the worst evil of all, as it will kill him or make him a chronic invalid from urinary sepsis.

There is no danger of injuring the peritoneum if the bladder is distended and the catheter inserted obliquely. The specimen illustrated in fig. 8, p. 7, shows the track taken by the catheter. This patient died from carcinoma of the bronchus with spinal secondaries sixteen days after suprapubic catheterization for paralytic retention: the bladder is neither contracted nor overdistended and it is clean. The peritoneal reflexion is an inch away from the track and was a good deal more when the catheter was put into the distended bladder. The length and obliquity of the track and its small size prevent leakage and make it the best substitute for the natural urethra which is, at least temporarily, out of action. The operation is easy and rapid: it should not be done until the bladder is distended but it does not require the perfect surgical surroundings needed for an open operation or for urethral catheterization. Incidentally it is the best. way of decompressing the bladder in cases of long-standing chronic retention from prostatic obstruction.

In conclusion, although there are still many gaps in our knowledge of the paralysed bladder we should be quite clear on the aims of our treatment. They are not only to prevent serious infection but to leave the patient continent, with a bladder which will hold an adequate quantity of urine whether it is passed voluntarily. or automatically or through a suprapubic tube.

REFERENCES

BARRINGTON, F. J. F. (1915) *Quart. J. exp. Physiol.*, 8, 33.
BURNS, J. E. (1917) *Surg. Gynec. Obstet.*, 24, 659.
EMMETT, J. L., and BEARE, J. B. (1941) *J. Amer. med. Ass.*, 117, 1930.
INGRAHAM, F. D., and SWAN, H. (1943) *New Eng . J. Med.*, 228, 559.
LANGWORTHY, O. R., KOLB, L. C., and LEWIS, L. G. (1940) Physiology of Micturition, Baltimore.
MACALPINE, J. B. (1934) *Proc. R. Soc. Med.*, 28, 39.
MERTZ, H. O., and SMITH, L. A. (1930) *J. Urol.*, 24, 41.
RICHES, E. W. (1943*a*) *Lancet* (ii), 128.
—— (1943*b*) *Brit. J. Surg.*, 31, 135.

Clinical Section

President—J. D. ROLLESTON, M.D.

[*November* 12, 1943]

MEETING AT ST. MARY ABBOTS HOSPITAL LONDON

Hæmolytic Hypochromic Megalocytic Anæmia Associated With Post-malarial Splenomegaly.—G. W. GOODHART, M.D. (Case reported by HAMILTON FAIRLEY, M.D., in *Trans. R. Soc. Trop. Med.*, 1940, 34, 173).

Male, aged 25, born in Bengal.

First attack of malaria at 2 followed by recurrences. 1922: Three weeks' fever with anæmia regarded as pernicious type. 1924: Enlarged spleen noted. 1928: Severe anæmia (Hb. 30%): dramatic response to cooked liver (Hb. to 75%). 1930: Fever and anæmia. Benign tertian parasites found. Satisfactory response to oral administration of liver extract. 1938: Arrived in England; worked hard on inadequate diet and complained of drowsiness, breathlessness and swelling of the ankles. Admitted to hospital September (1938) with severe anæmia which responded to treatment with crude liver extract (oral). Splenectomy performed; subsequently developed hæmolytic erythroblastic megalocytic anæmia with great increase in target cells and decreased fragility to hypotonic saline. Methæmalbuminæmia disappeared after splenectomy but reappeared later.

During past three years has carried on taking such liver extracts as were obtainable, the hæmoglobin percentage varying between 40 and 60. Other striking features during this period were the very large size of the red cells, the low colour index and the enormous numbers of nucleated red cells. Was twice admitted to hospital subsequently with relapses of grave anæmia, breathlessness and dropsy and responded well to blood transfusions. No response at any time to parenteral liver extracts.

On last admission spleen felt 2 in. below costal margin, presumably due to regeneration of splenunculus.

	R.B.C. in millions	Hb.%	Colour index	Diameter of red cells	White cells per c.mm.	Nucleated red cells per c.mm.
On arrival in Hospital for Tropical Diseases :—						
13.9.38	1·17	16	0·6	7·1		
During treatment :—						
11.11.38	2·93	40	0·7	7·5		
29.11.38	4·34	54	0·7	6·9		
(Splenectomy 26.1.39) :—						
8.2.39	5·54	76	0·7	7·2		
21.11.39	4·20	60	0·7	8·92		
2.9.40	2·47	30	0·62	8·2		
5.9.40		16				
Blood transfusion 500 c.c. :—						
7.9.40	2·57	28	0·56			
18.9.40	3·8	46	0·6		? 4,760	17,900
30.9.40	4·3	38	0·44			
26.10.40	5·7	54	0·5		8,740	14,260
14.11.40	6·5	58	0·44		11,000	88,000
29.4.41	3·89	40	0·51	8·6	32,000	125,000
22.5.41	4·24	45	0·54		19,000	180,000
30.12.42	3·0	42	0·7		11,000	
27.8.43	2·13	28	0·68		18,900	65,000
Blood transfusion 2 pints :—						
28.8.43		50				
Blood transfusion 2 pints :—						
8.9.43		74				
11.10.43	4·7	68	0·85	8·4	37,000	135,000

Dr. **Eli Davis** referred to the progressive increase in size of the red cells which the patient had shown following splenectomy.

He had under his observation a patient suffering from thrombocytopenia combined with hæmolytic anæmia whose spleen had been removed sixteen months previously and whose red cells had subsequently increased in size to a marked extent.

Unlike Dr. Goodhart's case his patient had not had liver treatment but had taken iron and marmite daily.

Dr. **F. Parkes Weber** said he did not know of any case exactly like Dr. Goodhart's. A feature which particularly interested him was the high degree of the symptom which he preferred to call "Erythroblastæmia" (*Lancet*, 1940 (i), 1077). He supposed that some

(presumably hæmolytic) agent was provoking an erythropoietic reaction by which a great number of immature (nucleated) red cells found their way from the bone-marrow into the circulating blood. There was, he understood, no evidence of the presence of excessive immature white cells in the peripheral blood.

Ulcerative Colitis, Treated by Medication Through a Cæcostomy.—JULIUS BURNFORD, M.B.

M. R., female, aged 31. Admitted to hospital 1936 with acute colitis. Persistent dysenteric flux, with much exhaustion. As the appendix had been removed some time previously, a cæcostomy was performed and a catheter inserted. Through this she was treated with oxygen at first and then with cod-liver oil daily. Otherwise her treatment included a generous dietary regardless of roughage, hydrochloric acid with the meals to counteract the deficiency of acid which is found in most cases, and isogel or normacol daily. She rapidly improved and became pregnant, but it was decided to remove the fœtus. A year ago she gave birth to a healthy boy without difficulty or inconvenience during the pregnancy. She occasionally has a mild relapse with inflammatory flux but this rapidly subsides with instillation of cod-liver oil through the catheter, which has been retained. Improvement in colon confirmed by X-ray examination (films shown).

AUTHOR'S NOTE.—The case is one of a large series of colitis treated with satisfactory results by appendicostomy and colonic medication.

Granular Leucopenia.—B. BARLING, M.D.

E. R., female, aged 26. For twelve years has complained of ulcers in the mouth, recurring at irregular intervals of three to four weeks.

Blood-count 1941 showed total white cells 2,600 with 40% polymorphs; series of counts showed that appearance of ulcers coincided with low white cell counts. No relationship between ulcers and menstrual cycle. Fractional test meal normal. Ulcers are shallow and appear on tongue or inside of mouth and are sufficiently painful to make mastication difficult. No response to any form of treatment to date.

Dr. F. Parkes Weber said he had no evidence that in the extremely rare cases of this class there was a spontaneous tendency for the attacks to cease to recur. There was indeed, he thought, a question of the advisability of trying splenectomy later on. One might compare D. Embleton's case of "Rhythmical Neutropenia with Recurrent Buccal Ulceration" in a woman, aged 43 (*Proc. Roy. Soc. Med.*, 1937, 30, 980).

Strangulated Uterus in Inguinal Hernia.—R. LAIRD, Ch.M.

E. W., female, aged 41.

History of hernia in right inguinal region for fourteen years, reducible until shortly after the birth of her youngest child four years ago. Two days before admission to hospital swelling increased in size and became painful. Last menstrual period fourteen days before.

Examination on admission.—An irregular mass, the size of a grapefruit, was found lying over inner half of inguinal ligament. No impulse on coughing; tender on palpation.

At operation fluid was found in the hernial sac which also contained an enlarged uterus, both ovaries and tubes. Subtotal hysterectomy performed outside the abdomen, the ovaries being replaced. Patient's post-operative progress was satisfactory.

Pathological report on the uterus showed early pregnancy.

Acute Hæmolytic Anæmia of Childhood.—C. A. ROYDE, M.B., and V. GLASS, M.B.

J. C., female, aged 7 (Gibraltarian parents).—Acute onset of shivering, headache and tingling of fingers.

On admission, within twenty-four hours of onset, very marked pallor but no other physical signs. Temperature 101° F., pulse 130. Hb. 30%; blood picture that of very active blood regeneration. Slight icteric tinge with 2·7 units of bilirubin and delayed direct Van den Bergh.

A small transfusion (250 c.c.) of stored blood (Group O) appeared to produce temporary improvement, but Hb. fell to a low level within a few days. During next seven weeks had repeated acute attacks of severe pyrexia, tachycardia and rigors with blanching and later icterus and splenomegaly: all these attacks appeared to be relieved by transfusion of stored blood.

July 1943: Had a continuous series of attacks *not* relieved by transfusions.

Operation.—Laparotomy 16.7.43 and large spleen (200 g.) removed.

One further hæmolytic attack ensued; treated by transfusion.

Has been much improved until recently but is now having a slow hæmolysis.

Has been on iron and cooked liver since admission.

Dr. **Herbert Levy** suggested that in view of the Gibraltarian origin of this child, the parents' blood should be examined for target cells: Dameshek had recently described (*Amer. J. med. Sci.*, 1943, 205, 643) the presence of target cells as the only abnormality in the parents of children suffering from Cooley's anæmia.

Pneumonectomy for Bronchial Carcinoma.—R. LAIRD, Ch.M.

F. K., female, aged 50. Admitted to hospital complaining of cough and pain in right chest. History of several small hæmoptyses.

X-ray of chest: Shadow at right base suggesting carcinoma. Bronchography unsuccessful. Patient was referred to Thoracic Surgical Unit, December 1936. Bronchoscopy showed carina of right bronchus narrowed to a pin-point lumen. Report on specimen removed for pathological examination: Trabecular, polygonal and oat-celled carcinoma of bronchus.

Dissection pneumonectomy 4.2.37 (Mr. Tudor Edwards) under high spinal anæsthesia. Incision anterior, below the right breast. Adhesions divided and lung removed after structure of hilum had been ligatured and divided. No carcinomatous glands seen.

Patient's post-operative condition satisfactory. Aspiration of chest gave blood-stained fluid.

Generalized Ossifying Chondromata.—LESLIE W. FRASER, M.B.

A. B., female, aged 70. Admitted to hospital 18.6.36 and found to be completely helpless owing to tumours of long bones. Never able to walk and always incontinent. Increase in size of tumours at intervals causing considerable pain.

No relevant family history.

On examination.—Large tumours on long bones ranging from size of an orange to that of a melon. Elbows fixed in 30 degrees flexion; slight to-and-fro movements at the right shoulder, no movement at left. Both thighs grossly enlarged. Both legs immobile and deformed by curvature to left. No sensory loss; knee-jerks not obtained; plantar reflexes flexor. Other systems normal.

Blood chemistry.—Blood calcium, phosphorus and phosphatase normal.

X-ray report (Dr. Grace Batten): The radiological findings in this case are extreme cystic expansion of all the long bones, apparently slowly progressive and primarily at the ends of the bones. In addition there is ossification of the main spinal ligaments and the right ischio-sacral, and ankylosis of the sacro-iliac joints. The condition of the long bones can probably be interpreted as a generalized ossifying chondroma of an unusually advanced type, and the associated appearances of spondylitis ankylopoietica are also a part of the disturbed calcium metabolism.

Huntington's Chorea.—G. A. JAMES, M.B., B.S.

J. C., female, aged 57. Admitted 5.8.42.

History.—Increasing difficulty in walking, inability to keep still and falling about for four years. In last three months has had several outbursts of temper. No family history of chorea.

On examination.—Cardiovascular, respiratory and alimentary systems: N.A.D. C.N.S.: Constant choreiform movements affecting the whole body. Speech markedly impaired by these movements. Mentality somewhat impaired, cheerful, fatuous but very independent. Cranial nerves intact. No nystagmus. Motor system: All movements normal but jerky. All reflexes rather brisk. Plantars flexor. Sensory system normal. No Rombergism. Special investigations: Blood W.R. and Kahn test negative. C..S.F.: traumatic bleeding at lumbar puncture. Normal fluid apart from this.

Unilateral Paralysis Agitans with Molluscum Fibrosum.—LESLIE W. FRASER, M.B.

A. K., female, aged 66. Unilateral (left) paralysis agitans showing characteristic cog-wheel rigidity and weakness with unilateral masklike expression and fine rhythmical tremor of twenty years' duration. Slight tremor of right hand during recent years if worried or excited; C.N.S. otherwise intact. Whole body surface covered with thousands of soft painless nodules in skin varying in size up to half an inch in diameter. Most of nodules sessile but some pedunculated. Marked pigmentation of skin. Blood-pressure 180/90. Blood W.R. and Kahn test negative. X-ray of skull: No evidence of abnormality in vault. A semi-opaque rounded shadow in left side and lateral parietal region—probably not bony.

Family history.—Mother epileptic with less marked degree of molluscum fibrosum.

Double Aortic Aneurysm.—C. A. ROYDE, M.B.

A. G., male, aged 79. Admitted with pain in chest and left shoulder on exercise, relieved by rest.

On examination.—Large pulsating tumour in left upper chest just lateral to angle of Louis. Diffuse apex beat 6th left space mid-axillary line; systolic murmur at apex. To-and-fro murmurs over aortic and pulmonary bases and over tumour. Blood-pressure: Left arm 200/100; right arm 180/70. Pupils eccentric and slightly irregular. W.R. + +. X-ray chest: Double aortic aneurysm of descending aorta.

Old Cystic Disease Right Humerus.—A. D. WINTON JONES, F.R.C.S.

P. E., male, aged 14.

History.—First attended January 1941 having been hit by a snowball containing a stone. X-ray: Spiral fracture of shaft of right humerus; position good. Fracture did not unite and when second X-ray taken cystic condition of shaft suspected. Following month sustained ⁻pathological ⁻fracture⁻ of right humerus caused by throwing a ball. X-ray: Simple bone cyst with new crack running from cyst into old fracture.

July 1941: Third fracture following a fall. X-rays showed this to be through another cystic area higher up than the previous fracture.

The present condition is that all three fractures have united but repeated X-rays show that the cystic condition is still present in the humerus, although more localized. X-rays of pelvis, femora, tibiæ and skull show no evidence of any cystic condition.

Old Fracture Coronoid Process.—A. D. WINTON JONES, F.R.C.S.

J. L., male, aged 49. First attended 14.1.43 following fall down twenty steps injuring left arm. Examination and X-ray showed dislocated elbow-joint (postero-lateral). Reduction performed without particular difficulty. Post-reduction X-ray showed fracture of the coronoid process. In spite of the period of rest followed by gentle active movements myositis ossificans developed. At present left forearm is fixed in semi-pronation and there is very little movement.

Fractured Patella Excision.—A. D. WINTON JONES, F.R.C.S.

E. T., female, aged 60. First attended 9.2.42 for an injury to her left knee from catching her foot in a piece of string and falling forward on to her left knee. X-ray: Transverse fracture of the patella with wide separation. No sign of old injury. (Fracture of same knee five years ago.) Operation a few days later showed comminution at the site of the fracture. Patella excised; quadriceps aponeurosis apposed with interrupted silk sutures. Plaster applied. Subsequently physiotherapy to the knee was carried out and good movement and stability were obtained.

Paget's Disease of the Bone with Pathological Fractured Femur.—A. D. WINTON JONES, F.R.C.S.

C. S., aged 54. First attended on 6.2.43 complaining of pain in the left hip for two weeks. Also a swelling in front of the thigh. On the day of admission, slipped and fell, hurting the leg.

On examination.—Pale and shocked, left leg everted with large oval swelling in front of thigh, rather tender. Diagnosis: Fractured left femur. X-ray showed pathological fracture upper third of left femur due to osteitis deformans. Traction applied on a Thomas' splint and angulation deformity improved. Progress: Union very slow. Eventually a walking calliper was applied which the patient is still wearing.

(Other cases shown at this meeting will be published in the next issue of the *Proceedings* of the Clinical Section.)

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*October* 22, 1943]

An Examination of the Place of the Doctor in the State from Ancient Times to the Present Day, together with Certain Speculations Regarding the Future. [*Greatly Abridged*]

PRESIDENT'S ADDRESS

By Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P., K.H.P.

WE are all conscious to-day of living in one of those crises in the history of human society in which a phase of steady progress is replaced by a sudden jerk forward under the influence of a great social upheaval, in this case, as so often, war. We all hope that a more beautiful Society may emerge like the dragon-fly from the old cramping larval skin and, having balanced perilously for a while in imminent danger of drowning, the new being may spread its wings and take flight into the sunshine of a wider and better life. In that life Medicine must play a part—a more vital part than ever before, and it is this realization that has set our profession and the Nation in general to examining, though not always with all the fearlessness and objectivity which it deserves, the future relationship of the Doctor to the State.

In the course of my own examination of this question I have asked myself what has been in the past the position of the doctor in the community and the attitude of the public towards him, to what extent has the State concerned itself with his activities and what has our great profession done to regulate its training and conduct so as best to serve the community. Any attempt to answer this question in full would involve a review not only of the whole history of medicine, but also that of the many different civilizations which gave birth to it and conditioned its development, and such an account cannot be compressed within the narrow limits of a Presidential Address. I must therefore content myself to-day with glancing briefly at the medical profession in bygone ages and the public's attitude towards it, endeavouring to show how never-changing human nature causes a recurrence age after age of certain social tendencies and their resulting phenomena and how, in spite of our justifiable pride in modern scientific achievement and our youthful impatience with the past, we can yet use that past as a firm foundation for future progress and a warning of the pitfalls which may beset our path.

For convenience I propose to consider the position of the doctor in different civilizations and epochs taken *seriatim*, but I would ask you to bear in mind that these civilizations often overlapped.

The Medicine-Man

In the most primitive form of society the medical practitioner is represented by the "medicine-man", though in truth this personage is far more than a doctor in the modern sense of the word, fulfilling in addition the roles of priest, magician and sometimes chieftain. We are, perhaps, too much inclined to regard with amused contempt this father of our craft, but his importance is defended with convincing argument and almost affectionate vigour by Sir James Frazer in "The Golden Bough". . . . "The development of such a class of functionaries", he says, "is of great importance for the political as well as the religious evolution of society. . . . The profession . . . draws into its ranks some of the ablest and most ambitious men of the tribe, because it holds out to them a prospect of honour, wealth and power such as hardly any other career could offer" [1]. Admittedly the men who thus come to wield the supreme power in the tribe are those possessed not only of the keenest intelligence but also of the most unscrupulous characters, but Frazer maintains that nevertheless: "If we could balance the harm they do by their knavery against the benefits they confer by their superior sagacity, it might well be found that the good greatly outweighed the evil." . . .

Personally I am inclined to agree with Frazer that "the original institution of this class of man has, take it all in all, been productive of incalculable good to humanity. They were the direct predecessors, not merely of our physicians and surgeons, but of our investigators and discoverers in every branch of natural science".

JAN.—EPID. 1

It is curious to reflect that it is in this, the most primitive form of organized society, that we find the doctor occupying the highest position in the whole of history—and that never was the choice of doctor less free!

China

Chronologically the rival claims of China, Mesopotamia and Egypt to be considered next are difficult to determine, but I propose to take China as ancient Chinese civilization is to all appearances such an isolated phenomenon.

In the early phases of Chinese civilization which enshrine the memory of Shen Nung, the Divine Husbandman (supposed to have reigned 2838-2698 B.C.), still worshipped by native drug guilds as their patron god and venerated as the Father of Medicine, the profession was represented by priests and sorcerers and it was not until the Chou dynasty (1123-256 B.C.), one of the most glorious periods in Chinese history, that the functions of the two were separated. But unfortunately no amount of intellectual dexterity or philosophical insight can compensate for lack of scientific method and consequently medicine at this time degenerated from a practical art, based upon knowledge and observation, however restricted, into an absurdly elaborate and meretricious system, ever growing in complexity as it decreased in rationality and effectiveness. Very similar phases occurred in other and later civilizations as I shall hope to show. However we may venerate China as the birthplace of systematic medicine, the medical student must ever bear her a grudge for inventing medical examinations, which appear in China as early as the tenth century B.C. In contrast to the scholastic atmosphere of the Chou dynasty these early examinations were devised on a very practical basis of grading by the percentage of successful cures, a system which persisted without material change into the T'ang dynasty (A.D. 618-906). It would, however, be a mistake to conceive of medical education and testing at this period as provided on a national scale. Medical education was confined almost entirely to the Imperial College, an institution whose purpose was to care for the needs of the Emperor rather than to train doctors to look after his subjects. It was not until the Sung dynasty that proper medical schools were established, first in the capital and later in other parts of the country, and the scope of the examinations markedly widened till they corresponded nearly to the official literary competitive examinations which for long ages played so important a part in the intellectual and official life of the country. . . .

In the third year of Yiu Yu (A.D. 1317) State medical examinations were reintroduced and under the same dynasty women doctors were officially recognized for the first time.

The Chinese people are famous, among other qualities, for their love of order and nothing in the history of Chinese medicine is perhaps more remarkable than the high degree of practical organization which existed side by side with extremely artificial medical theories during the Chou dynasty. The Chou Rituals describe four kinds of doctors, each with his special well-defined sphere. First there is the dietitian to look after food and drink; second the physician, concerned with internal complaints only; third the surgeon, whose sphere is external diseases such as wounds, fractures and ulcers; and lastly the veterinary surgeon to care for sick animals.

You will note that the dietitian comes first in this classification, and this is the place he occupies in the scheme of organization of the medical department. His function is defined very exactly as that of mixing the six foods and drinks, the six meals, the hundred sauces and the eight delicacies to see that each is of the right taste and consistency.

At this period, in spite of the fact that the priest and physician were already separate, there was still general distrust of the latter's ability and character.

The Analects says that without perseverance one cannot even become a doctor and the Record of Rates warns against taking any medicine compounded by a doctor who has not the experience of three generations behind him; an attitude of caution shared by no less a person than the great Confucius who, on being sent a present of medicine by a disciple received it with a bow and the words "I do not know it. I dare not taste it" [2]. The T'ang Annals class doctors with mathematicians, surveyors, fortune-tellers, physiognomists and magicians as charlatans. "The Sages", it says, "did not regard them as educated."

All Ancient Chinese writers do not, I am glad to say, take such a poor view of the profession, and perhaps the highest tribute paid to them was by Fan Wen-Chêng, of the Sung dynasty, who said that if he could not aspire to be a good statesman he would be a good doctor. Finally I would commend to your notice this very modern dictum of an ancient Chinese sage, Su Wen: "The sage does not treat those who are ill but those who are well." Is not that real preventive medicine?

Mesopotamia

The records as regards ' our profession in ancient Mesopotamia are extremely limited. Babylonic-Assyrian medicine was essentially demonistic and "primitive folk medicine, with all its superstitions, completely dominated the medical teaching of the ancient Babylonians" [13]. But religious influence was not, apparently, the only stumbling block in the path of the Babylonian doctor, he was in addition alternately encouraged and intimidated by a scale of rewards and punishments of an elaborate kind. The Code of Hammurapi (c. 2200 B.C.) which is almost entirely surgical lays down an award of ten shekels of silver (less than £1) for a successful major operation, the reward being reduced to five shekels in the case of a free man and two shekels from the owner of a slave so operated. If, however, the patient died or lost his eye the surgeon was to have his hands cut off, though if the patient was a slave the doctor merely had to replace him by another slave [3]. The beginnings of medical learning in Assyria probably date back to nearly 3000 B.C., but medical lore seems to have changed very little there even by the seventh century B.C. when we find Arad-Nanai, a famous medical man and court physician of Esarhaddon, the son of Sennacherib, writing letters to the king advising him on the treatment of his illness, probably rheumatism [14]. Babylonic-Assyrian medicine remained to the last demonistic and wedded to incantation and divination, but nevertheless, as Jastrow says, "the physicians of Babylonia and Assyria . . . passed across the barren wastes of incantation rites and divination practices and reached at least the border of the promised land of pure genuine medical science" [13]. Babylonia, however, "had nothing to teach Greece which could have led to the great schools of medicine associated with Cos and Cnidos".

Medes and Persians

After the fall of Babylon and the establishment by Cyrus of the kingdom of the Medes and Persians the records become even scarcer, almost the only source of information being the religious writings carefully preserved by the Parsees, namely the Zend-Avesta and its literary predecessors.

The Persians, like the Babylonians before them, had a scale of charges authorized for doctors—as well as a scale of punishments. Thus the Vendidad, or code of purifications of the Zend-Avesta, lays down that: "A priest must be healed for his blessing; the head of a house, a village, or a town for the price of an ox, of low, average or high value respectively, while the lord of a province must pay the price of a chariot and four" [4]. But when we come to the penalties for unsuccessful surgery a novel and interesting feature appears, namely the sharp distinction between operations upon believers (Mazdajasnas) and unbelievers (Daivajasnas). Medical students are enjoined to get their hand in by practising surgery on unbelievers and it was only when the budding doctor had killed three such that he was considered unfit to practise! If, however, he was skilful enough—or lucky enough—to perform three successful operations on these experimental subjects, he might be allowed to exercise his craft upon worshippers of Ahura-Mazda. If he dared to practise without passing this test and the patient died it was regarded as premeditated murder.

Even in these early days the special obligation of the physician to attend a patient promptly when called upon was clearly laid down, but coupled with this injunction was an admirable warning against hasty treatment before the symptoms had been carefully observed.

Persia's most valuable contribution to medicine arose from her geographical position, which enabled her to act as a bridge between the civilizations of the East and the West. Important among the countries whose medical learning and knowledge of drugs were thus transmitted to the Near East and eventually to Europe was India.

India

In India we find the status of the physician refreshingly elevated, at any rate during the Brahmanic epoch, the golden age of Indian medicine. This is accounted for by the fact that the physicians of this period were independent of the priesthood; belonged to a high mixed caste of Ambastha (Vaidya), descended on the father's side from Brahmans; were required to possess manual dexterity and certain physical, moral and intellectual qualities; and finally not only their scientific studies but also their whole mode of life, their relations with their patients and patients' friends and their fees, were all prescribed in the minutest detail. It is interesting to note, however, that as in Egypt and Imperial Rome (as I shall show later) the services of these superior practitioners were not at the disposal of the whole population. Hunters, fowlers, caste-breakers, criminals and incurables were not to be treated by them.

A remarkably sensible conception of the physician's role in the treatment of disease

is shown by the following passage from the Ayur-Veda of Susruta: "The physician, the patient, the medicine and the nurse are the four feet of medicine upon which the cure depends. When three of these are as they should be, then by their aid the exertions of the fourth, the physician, are of effect, and he can cure a sore disease in a short time" [4].

And what better tribute could any of us hope to earn than that contained in this description of the physician of ancient India: "In illness the physician is a father; in convalescence a friend; when health is restored, he is a guardian" [3].

Egypt

In Egypt we find the earliest physician known to history, Imhotep, medical adviser to a Pharaoh of the thirtieth century B.C., who as the Asclepios of the Greeks and the Aesculapius of the Romans became the patron god of medicine in early classical Europe [14].

In the early days of Egyptian civilization the priest-physician was the practitioner of medicine, but the differentiation of function occurs quite early resulting in the development of physicians, surgeons and exorcisers, the last named holding the highest position of the three. Further differentiation occurred as time went on, but it was not until Egyptian civilization, and with it Egyptian medicine, were on the decline that highly developed specialism occurred, as described by Herodotus. I shall refer again later to this association of specialism with social decay.

The death penalty attaching to a fatal outcome of medical treatment is found again in Egypt as in Mesopotamia and the Persian Kingdom. It is true that the medical practitioner was held to be free of blame in such cases so long as the treatment followed prescribed lines, but this rule, however comforting to the doctor, can hardly be regarded as an encouragement to progress.

One of the most remarkable features of the civilization of ancient Egypt was the manner in which every minute detail of public hygiene and private life was regulated by ordinance. The manner of life, the cleanliness of the house, the care of the body, clothing, diet, sexual life, all were exactly prescribed and in return for compliance long life, boundless health and many offspring were promised. "The whole manner of life", says Diodorus, "was so evenly ordered that it would appear as though it had been arranged according to the rules of health by a learned physician, rather than by a lawgiver" [3]. The same author tells us that the Egyptian physician was obliged to treat soldiers and travellers free of charge. In many respects Egypt was a pioneer and one can clearly trace her profound influence upon the Mosaic law and the beginning of medicine in Greece and through these on the whole subsequent course of civilization.

Hebrews

It was towards the end of the Hyskos dynasties in Egypt that Joseph entered the country and later Jacob and his Seventy Souls, and there the Hebrews remained for two hundred and ten years [5]. There is no need for me to remind you of the changes which took place in the position of the Hebrews in Egypt during this period, culminating in a state of profound unrest and decline during which Moses was born and brought up in the palace of the Pharaohs. Here, as he grew up, he eagerly absorbed the wisdom of ancient Egypt, neglected by her then rulers, and that the medical papyri must have particularly attracted his interest is shown by the remarkable hygienic laws which he gave to his people when he led them out of the land where they had been reduced to slavery. His fine intelligence, as well as the traditions of his race, led him to despise magic and magicians and, what is more remarkable, to disentangle the hygienic lore of Egypt from the religious symbolism and superstitious practices with which it had become encrusted.

The elaborate system of hygienic ordinances and public health officials (priests) which he devised, is familiar to all of us from the Old Testament.

In view of the criticism often levelled at the medical profession to-day of giving insufficient dietary advice to their patients, it is noteworthy that Moses was apparently not content merely to adopt the numerous and detailed dietetic rules he found in the Egyptian papyri, but carried out careful researches of his own, the results of which he embodied in his code. These rules concerned the selection, cleanly preparation, cooking, serving and eating of food and proved of inestimable value to his people, especially during their wanderings in the wilderness.

Later, when they became established in Palestine, medical science underwent some development and received special impetus from King Solomon, who is said himself to have written a book on the subject. The increasing influence of surrounding nations greatly enlarged the outlook of the Hebrews resulting in the evolution of lay doctors

in addition to the priests, and eventually even Gentile doctors were employed and Jewish doctors were obliged to care for Gentile patients when called upon [6]. These lay doctors gradually won a high place in Jewish society and medical officers were appointed for each town, and surgeons as well sometimes. The priests, too, had their special doctors.

Greece

At no point do I find it so hard to confine myself within the strict limits of my subject as when I reach the sunny shores of Greece, and am confronted by the amazing and fascinating picture of that great civilization to which we owe so much in every department of life and learning, and certainly not least in medicine. In the world's history there has been only one Hippocrates, of whom Dante says:

> ". . . quel sommo Ippocrate, che natura
> agli animali fe ch'ell'ha piu cari"
> (Purgatorio, Cant. XXIX. st. 137-8).

Of doctors in the early days we know little, but Homer tells us that they were held in high esteem, and even in this early period we hear of "lay physicians who freely exercised their profession, untrammelled by temple medicine" [3]. State medicine, too, was well organized, with towns appointing their official physicians at a fixed salary, to attend the poor without charge, to control epidemics and to give expert evidence in Court; and the army and navy had their own medical corps.

Freedom of entry into the profession—except for women—and freedom of practice for those duly qualified—with the exception that slaves might only treat slaves—encouraged progress in the art. The physician qualified by undergoing a practical and theoretical course of instruction under a recognized master and received a diploma which was essential for any doctor wishing to be elected (by popular assembly) to an official post. Physicians practised in their own homes or went on circuit. Besides domiciliary treatment there were nursing homes (*Iatreia*) provided with sick rooms for temporary treatment. Some of these *iatreia* were the property of the more eminent physicians, whilst others belonged to the community and were staffed by public medical officers. Such "homes", which were light and airy, were used chiefly for surgical operations and were equipped with all the necessary instruments and appliances.

Now let us consider for a moment who these physicians were. Though, as I have pointed out, there were lay physicians even in the very early days of Greek civilization the original Greek doctors were the priests of Aesculapius, the god of healing, who made a special study of the healing art. The temples of Aesculapius were built in beautiful surroundings, usually on high ground, and treatment was assisted by music and the drama. The priests of these temples were known as Asclepiades, but later this term was applied as well to the lay doctors working there. During the century preceding the birth of Hippocrates the Asclepiades of Cos and Cnidos developed into a sharply defined guild, bound together by common religious beliefs and scientific views and controlled by strict rules aimed at securing a high ethical standard in their relations with each other and with their patients. Brotherly love, gratitude to their teachers, duty to their patients and the preservation of their science from profanation by the vulgar—such were the guiding principles of this unique society, which 460 years before Christ gave us that unsurpassed medical genius, Hippocrates. . . .

In ancient Greece, as at the present day, there were not wanting laymen who, though not medically trained, did not hesitate to express views, often fantastic, on medical subjects. Among these was the great philosopher Plato (427-347 B.C.), but though his medical theories are not worth our notice his description of contemporary medical practice is of considerable interest. He tells us how the slave assistant of the free doctor attended on the slaves, either at home or in his master's consulting-room, prescribing empirical remedies without discussion, "like an unconstitutional monarch", whilst his master, attending free men, took great pains in his examination of his patient, consultation with his relations, and instructions as to treatment and regime [7]. Such differences in the medical care provided for different sections of the population persisted in all countries until quite modern times. But in spite of this blot on Greek medicine the rules of conduct for our profession, which are embodied in the famous Hippocratic oath, have survived until to-day as the standard of medical ethics. Before leaving, regretfully, this absorbing section of my subject, I must make brief reference to an event which proved to be epoch-making in the history of medicine, namely the founding of the famous School of Alexandria with its unique library of at first 50,000 and finally 700,000 volumes. This was the work of Ptolemy I, a general of Alexander the Great, whose tutor was Aristotle, the founder of the sciences of comparative anatomy and natural history. Medicine was an important subject in the School of Alexandria and was from about 300 to 200 B.C. based upon observation and ascertained facts in the true Hippocratic tradition, nothing contri-

buting more to medical progress here than the free practice of human dissection. But, alas, in the later years of the Alexandrian School a sad degeneration set in and the Hippocratic principles were smothered by a mass of unscientific and pedantic speculation.

Rome

Ancient Rome provided a much poorer soil than Greece for the cultivation of medical science. Medical practitioners are recorded in Rome in very early times, for instance the Lex Emilia, passed in 433 B.C. ordained punishment for the doctor who neglected a sick slave and Dionysius of Halicarnassus mentions physicians in the epidemic of 451 B.C. But the native Roman doctors do not appear to have been either well trained or distinguished by their character or skill. They took no regular course of study, but acquired their knowledge through apprenticeship to a practitioner to whom an honorarium was paid. Pliny's remarks deploring the want of medical education and the credulity of the public are well known and perhaps it was just as well that the heads of families were the chief physicians of the time, having wide powers over the members of their households conferred upon them by Roman law.

The medical art made no real progress in Rome until Greek medicine became firmly rooted and this did not occur without considerable difficulty and many setbacks in spite of its manifest superiority to the native Roman brand. Jealousy of foreigners and especially of the Greeks, many of whom where indeed unscrupulous charlatans, long delayed the naturalization of Hellenic medicine in its new home, but this was finally accomplished by Asclepiades of Prusa at the beginning of the first century B.C. With the coming of the Augustan age we find the doctor still occupying a very low place in a society consisting of a small tyrannical, debauched, and superstitious upper class and a large thriftless and degraded lower class. Rome was the happy hunting ground of quacks. Some of the practitioners were slaves, appointed by the heads of great households to look after the other slaves of the house, but the majority were freedmen who practised in booths, in which they prescribed and compounded with the aid of freedmen and slaves who were their assistants and pupils.

By the time of Constantine the two classes of *archiatri* had become established, namely the *archiatri sancti palati*, or court physicians, and the *archiatri populares* who attended the people. Each of the regions of the city had its own *archiater*, except for those of the vestal virgins and the gladiators which had their own special medical officers (Galen was one of the latter). These *archiatri*, especially the *archiatri sancti palati*, were given numerous privileges, such as freedom from taxation and from the billeting of soldiers on them and immunity from imprisonment. The *archiatri populares* were elected by the people themselves and paid by the Government a basic salary for attendance on the poor, but were not debarred from private practice, which often proved very lucrative....

With the death of Paulus Aegineta, a famous Greek physician of the seventh century, a rapid and marked decline in the practice of medicine and surgery set in and lasted for five centuries.

Arabian Medicine

I must now consider very briefly the position of the doctor in the important period of Arabian Medicine beginning at the end of the eighth century A.D. Though only one important medical writer of this period, Al-Kindi, was of Arab stock, the rest being Persians, Syrians and Saracens of the Western Caliphate and Jews [8], yet Arabic was the medium employed by all. When Roman civilization in Europe was overwhelmed by the barbarians, Arabian medicine, by preserving some of the Greek writings and by its own original contributions, kept the flame alight. The Moslems put tremendous enthusiasm into the task of translating the Greek authors and Baghdad, capital of the Islamic Empire, became a great centre of learning. There, about the middle of the sixth century, the school of Djondisabour was founded, and for several centuries the school and its attached hospital occupied the front rank in the world of medicine and science, supplying physicians to Persia, Irak and Syria. The greatest impetus to the work of the school was given by Ala Mamoun, son of Haroun al Raschid, who started the movement for the translation of the Greek authors.

Islam, in its spread westwards to North Africa, Sicily, Southern Italy and Spain, carried this learning with it.

Spain, where the Arabs had become firmly established about A.D. 711, became especially famous throughout Europe for its medical lore and students flocked there from all parts. When the Omniade Sultan, Abdurrhaman, a contemporary of the famous Abbaside Sultan al Mansur, set up his banner of independence at Cordova in 758 he encouraged with commendable zeal the pursuit of medical and other learning, and under his successors this city became the Baghdad of the West, where thousands of eager students studied

science with the help of a rich library. One of the great services given to the medical world by the Arabs was the establishment of well-endowed hospitals (of which the one in Baghdad, to which I have referred, was the first) where carefully supervised medical teaching was given on very practical lines. An examination system was also developed with the object of testing the capacity of the student before allowing him to practise. Unfortunately this system does not seem to have established any permanent footing.

Before leaving the subject of Arabian Medicine I must refer to one of the earliest medical examinations on record. In 931 a doctor in Baghdad killed a patient through carelessness. In consequence of this the Caliph required all doctors, except the Court physicians and those of recognized ability, to submit themselves to examination [6].

MIDDLE AGES

I turn now to the Middle Ages, and this is, perhaps, an appropriate place in which to note an important change wrought by Christianity in medical ethics. Even the Hippocratic rule enjoined the doctor not to treat "incurable" cases, but Christianity reversed this. As Neuburger says: "die Humanitätsideen des Christentums, mit ihrer hohen Einschätzung des Menschenlebens, machten ihm hingegen seinen Beistand auch in diesen Fällen zur sittlichen Pflicht."

I would say a word first about the doctor found among the most primitive European peoples of the time. The most backward of all, perhaps, were the Germanic tribes, especially those in North Germany and Scandinavia where the physician, known as *lachner*, was a mere medicine man and demon-chaser, practising strange and horrible rites including human sacrifice. The Riparian and Salic Franks were definitely more advanced and appointed public medical officers (among whose functions was the determination of virginity) and also established hospitals under lay control, such as the one founded at Lyons in 542. Among the Celtic Gauls the doctor was at first also a priest, a Druid, but by the seventh century medical practice was largely in the hands of laymen, who were regarded as craftsmen rather than scholars. These men were itinerant, and the surgeons long remained so, but medicine (as distinct from surgery) was gradually transferred to the monks, though throughout the first half of the Middle Ages many Jews and a few Arabs practised in Southern Europe [8]. England, I am sorry to say, lagged far behind Italy or even France during the first part of this period, but Scotland was more advanced as it had a peculiar type of hereditary physician in the great families, the origin of whom is to be traced to Ireland which was at this time tranquil, and a home for monastic learning and the preservation of classical tradition.

But the real springs of medical learning in mediæval Europe were to be found in Spain and Italy. I have already referred to Arabian medicine in Spain, and I would only add now that there were also many Saracen physicians practising in Sicily and Southern Italy. Apart from Saracens and Jews the teaching of medicine was mostly in the hands of the monks and other clerics who were, indeed, practically the only educated class. It is all the more remarkable, therefore, that Salerno, Europe's first real school of medicine, and for long the only one, should have been from the beginning under lay control. Before this time, however, some medical knowledge had been preserved and handed down by the monks who looked after their sick brothers, though the real awakening in the monasteries of interest in medicine can be dated to the founding of the Monastery of Monte Cassino by St. Benedict of Nursia in 529. This centre of learning reached the peak of its fame towards the end of the ninth century, being then eclipsed by the neighbouring School of Salerno, the first European university. The story of Salerno has till recently been "wrapped in the mists that shroud the dawn of learning" [15] but these mists have been largely dispelled lately by the work of Professor Sudhoff. One of the secrets of Salerno's success appears to have been the thoroughness and efficiency of the instruction given. In 1140 King Roger of the Two Sicilies decreed that no physician should practise medicine in his kingdom before receiving authority from the royal officials, and this is probably the first medical practice act in history [8]. But it was Roger's grandson, Frederick II, nicknamed in the Middle Ages "Stupor Mundi" who, when founding his new university at Naples in 1224, with extraordinary vision, laid down rules, which even to-day do not seem very old-fashioned, for the regulation of medical teaching and practice. These rules required the budding doctor to pursue a three years' pre-medical course in philosophy and literature, followed by a five years' professional course and a year's apprenticeship to an experienced practitioner. Finally he was examined on the genuine works of Hippocrates and Avicenna (which had been introduced about 1077 from Africa by Constantinus Africanus, the arch-forger who inaugurated the new age of medicine in Europe) and if he passed this test and produced the requisite testimonials a formal graduation ceremony set the seal upon his qualifications. The code, it may be

noted, provided for the education of poor students free of charge. It also laid down a scale of fees to be charged by practitioners and placed druggists and apothecaries under the control of physicians, who were strictly forbidden to have any money transactions with them. The new University practically killed Salerno [16]. . . .

Before leaving Italy some mention must be made of the guild of physicians and apothecaries established in Florence in the twelfth century and . . . which numbered Dante Alighieri and Collucio Salutati among its members. A Statute of 1314, prescribed examinations, for a licence to practise, by the Consuls of the Guild. . . . Later statutes ... prescribed for qualified practitioners their scale of fees and rules of conduct. Florence from a very early period employed salaried physicians and surgeons to attend the poor without charge. But on this fair picture appeared once more the blot I have referred to in Egypt and Ancient Rome—over-specialization founded on insufficient knowledge.

Let us now pass to France. Here monastic medicine reached its height in the tenth century, though surgery was left much freer owing to the traditional prejudice of the Church against shedding blood. The decline of monastic medicine was due to many factors, among them the establishment of the Cathedral Schools . . . these schools, though in clerical hands, being much freer than the monasteries; . . . Let me take the Faculty of Medicine of the University of Paris as an example. This Faculty started on the second floor of a house in the Vicus Straminus (Straw Street), on the first floor of which prostitutes plied their trade. Here the lecturers and pupils alike sat on the floor but later, when the Faculty moved to the Rue du Fouarre, the professor was promoted to a wooden stool, though the students still sat on the ground and wrote on their knees, an arrangement of which Pope Urban V in 1366 wrote approvingly because it encouraged humility. The course of instruction too was long and hard, starting in the summer at five, and in the winter at six, in the morning. The minimum length of the course in the fifteenth century was six years, of which two were spent in acquiring a Master of Arts degree. The medical course was punctuated by a series of examinations, of which those for the lower degrees of bachelor and licentiate were partly practical, but those for master and especially doctor were purely academic. Only the degree of doctor permitted independent practice. . . . The surgeons, in France, were not organized or regulated like the physicians until Jean Pitard, physician to St. Louis, founded the College of Surgeons or Confrérie du Saint Côme. Under the rules of this corporation no surgeon was allowed to practise until he had passed a rigorous examination by the College, which was authorized to confer the lower degrees, but not that of doctor.

Now at long last we reach England, where the evolution of medicine was on much the same lines as in France, terminating in the establishment of the Cathedral School at Canterbury, which somehow never developed into a University, and then in the gradual evolution of the medical faculties at Oxford and Cambridge. The University of Oxford, founded in 1206, may be regarded as a daughter of the University of Paris. In the thirteenth century both the masters and the students at Oxford, as at Paris, were clerics wearing clerical garb and the tonsure. At Cambridge, recognized by royal charter in 1217, the progress of medicine was very similar to that at Oxford. . . . The medical course at Oxford was much the same as I have already described at Paris and the discipline was as strict. A high standard of competence was required for medical graduation. . . . All the same the knowledge required of candidates in the thirteenth and fourteenth centuries was apparently entirely theoretical, culled from the works of Hippocrates, Galen, Isaac and Nicolaus, and no mention is made of clinical experience or anatomical knowledge. *No surgery as such was taught at either Oxford or Cambridge until the fifteenth century.*

Now what was the attitude of the public towards the doctor in the Middle Ages? There were many who ridiculed them. "Trop croire physique c'est folie" says Perrot de Saint-Cloot. Petrarch's strictures, though perhaps unusually scathing, typify the attitude of the educated public of the time towards the doctor. In the brochure "Contra Medicum quendam Invectivæ" he writes: "The physician loses sight of the real needs of the sick and in order to bring health he fills him with syllogisms. Formerly one treated the sick without philosophizing too much. Now artificial conclusions are drawn and the patient remains sick. Many thousands die while the physicians argue and perorate" [8].

That medicine, including surgery, was an occupation with very special risks in the early part of the Middle Ages is shown by the fact that in the fifteenth century Pope John XXII burned an unsuccessful physician at Florence, and on this Pope's death his friends flayed alive the surgeon who had failed to keep him alive.

POST-MEDIEVAL ENGLAND

In the remainder of this account of the history of the doctor I propose to confine myself to this country. In the third year of King Henry VIII an Act was passed limiting the

practice of medicine to such persons as should be duly examined and approved, the pre-amble stating that medicine was being practised by a "great multitude of ignorant persons, of whom the great part have no manner of insight in the same, nor in any kind of learning", and stating that these quacks included "common artificers, as smiths, weavers and women". Practice was therefore limited within the City of London, or within seven miles of it, to those examined, approved and admitted by the Bishop of London or the Dean of St. Paul's assisted by four doctors of physic, or for surgery other expert persons. Outside London and its precincts the examinations and admissions were to be in the hands of the bishop of each diocese also assisted by experts. In the tenth year of his reign this enlightened monarch at the instigation of Thomas Linacre, founded the Royal College of Physicians of London, the letters patent being dated September 23, 1518. The powers given to the new College were very wide, and included not only holding examinations and granting licences to practise but also punishing offenders by means of fines or imprisonment. Five years later further powers were granted and the new Act provided that, except for graduates of Oxford and Cambridge, no one should be allowed to practise physic in the whole of England without the authority of the College. In 1560, another Act gave the College control of the apothecaries' shops.

The complicated history of the evolution of the Royal College of Surgeons . . . has already been described by many able pens.

The position of the profession in mid-Tudor times is described by Simon as follows: "The medical profession had but imperfectly detached itself from other industries. Three main roots for it were discernible. Apothecary, surgeon, physician, each had a mark of his own; the first his familiarity with the uses of worts and drugs; the second his skill for bleeding, bandaging, bone-setting and the like; the third his book-learning, especially in the Greeks and Latins, and often his mastery of at least one occult science; but the apothecary was still a variety of grocer, the surgeon still a variety of barber, and the physician but just ceasing to be an ecclesiastic" [9].

The emergence of a learned profession, with its two distinct but related branches, from the Tudor phase is bound up with the development of the two Royal Colleges; but the legal constitution of the medical profession with the establishment of a Medical Register by which, for the first time, the public and its courts of justice were able to distinguish the qualified practitioners from pretenders, and the control of licensing bodies, had to wait for the Medical Act of 1858.

In the securing of this reform the Provincial Medical and Surgical Association—now the British Medical Association—played a leading part. This Act did not, however, remove completely the confusion due to many ports of entry nor did it establish a suffi-ciently democratic control of the profession. The amending Act of 1886, which, among other things, recognized the essential unity of the profession by demanding evidence of training in both medicine and surgery as a qualification for registration, improved the position substantially, though many people to-day, both inside and outside medicine, consider that a further reform of the General Medical Council is overdue.

Much has been written about the famous consultants of the eighteenth and nineteenth centuries, but . . . I will confine myself from now on to the general practitioner whose future is a matter of particular concern to us at the present time. Certain characteristics seem to have been common to the general practitioners of both the eighteenth and nine-teenth centuries. They were on the whole men of keen observation, of great independ-ence, and intimately acquainted with the lives of their patients, especially in the country and the smaller towns. These characteristics resulted partly from the truly scientific spirit infused into the profession by such great men as Harvey, Hunter and Sydenham, and partly from the greater intimacy of social life in general before the advent of fast and easy transport. Another important factor was the absence of the numerous labora-tory tests and other special investigations, upon which all but the wisest have become increasingly dependent, thus tending to lose some of that clinical acumen and self-reliance which not only directly benefited the patient but also won his confidence. Sir D'Arcy Power describing the career of the average man on qualification in the 1870's says: "As a rule he settled down in his native place and became the highly respected, but ill-paid doctor with many club patients. By day and by night, in all weathers, he drove in a high dog-cart sheltered by a large umbrella held by his groom. The wise doctor went on horseback" [10]. . . .

Almost within the lifetime of some of my distinguished audience two great changes have occurred which have profoundly affected the life and work of the general practitioner. First there is the wonderful series of discoveries and inventions in physics and chemistry, which have enlarged so enormously the horizon of medicine and the possibilities of diagnosis and treatment—a change for which we must all be devoutly thankful, but which is attended by the danger, to which I have just referred, of failure to see the

wood for the trees.   Secondly, there is the awakening of the social conscience to the demands of the public health and in consequence the ever-increasing concern of the State with the preventive aspects of medicine—or in current jargon "the achievement of positive health".   As Sir George Newman put it in his Heath Clark Lectures in 1931: "Between 1874 and 1930 Parliament imposed statutory duties of a preventive kind upon every registered medical practitioner.   He must certify, notify, and justify in various and manifold directions.   His liabilities as a certifying officer of Preventive Medicine have become comprehensive—birth, sickness, death; poisonings, vermin, vaccination; nuisances, disinfection, offensive and dangerous trades; inebriates, mental deficients, drug addicts" [11]. And, quoting Sir Henry Acland: "The general practitioner throughout the whole country became connected with a State system of organized medical observation and relief. . . . A new conception of Medicine had arisen throughout the English-speaking race."   Probably the most radical of these changes from the general practitioner's standpoint was that effected by the National Health Insurance Act of 1911. This measure was, in the words of Professor Thomas Fraser of Aberdeen, "revolutionary in character, and it is not surprising that the profession in the first instance saw itself threatened with a form of control entirely foreign to all its traditions, and on conditions dictated by the State with what was believed by practitioners to be an incomplete understanding of the work involved" [12]. No, the profession's fear of the Bill is not surprising.   What *is* surprising, to me at any rate, is that the once dreaded National Health Insurance system should have established itself so firmly in the affections of the profession in the last thirty-two years, that now a large section, apparently, regards the extension of its provisions to include practically the whole population as the most desirable way of meeting the public demand for a comprehensive national medical service.   Few people familiar with the conditions of general practice before 1911, would, it is true, doubt the benefit conferred by the Act on the general practitioner.   "In the days before the National Health Insurance Act", Fraser says, "the usual method of starting practice in Aberdeen was to put up a plate and wait for patients to appear—often a long wait.   To the young practitioner election as medical officer of a Society", that is to say a Friendly Society, "was a boon; it gave him work on which to build up a reputation and enlarge his experience.   The disadvantages, however, were many, among them undignified competition for such posts and no security of tenure. The proposed Act removed many of these disadvantages."

Apart from the medical care provided under this Act the State has in recent years taken steps to supervise the health of the school children and of expectant and nursing mothers and children under school age.   These services were committed to the care of Local Education Authorities, and of certain Local Sanitary Authorities respectively.   This is no place in which to discuss the rights and wrongs of the arrangements made for the staffing of the clinics where this work is done, and I will only remark that it is now pretty generally agreed that the separation of this work from the general medical supervision of the family is unfortunate from more than one point of view.   It can hardly be doubted, in fact, that the ideal arrangement would be continuous medical supervision of the individual from conception to death by the same person and the preservation of the family unit as the basis of the general practitioner's work.

I believe that one of the basic causes of the profession's mistrust in 1911, of the practitioner's failure to participate more fully in the personal health services provided by the State, and of much of the profession's fears as to the future, is the failure of medical education to keep pace with the swing over of medicine to the preventive side.   It is true that the General Medical Council recommended in 1922 "that throughout the whole period of study the attention of the student should be directed by his teachers to the importance of the preventive aspects of Medicine", but to what extent has that recommendation been implemented?   The reform of medical education is far too large a subject for me to discuss here, but I hope in a minute to give some indication of what I believe to be the need that it should meet, or in other words what position the general practitioner should occupy in the State of the future.

In the reflections and speculations which I am now about to offer you I would emphasize that I speak as an individual and that my views are not necessarily those of the great Department which I have the honour to serve.

REFLECTIONS AND SPECULATIONS

As Riesman says: "We can see far, because we are standing on the shoulders of our ancestors."   What, then, have we seen from that elevation which will help us in planning the future of medical practice?   First we have seen the doctor's evolution through many vicissitudes from the magician, through the priest and the tradesman, to the erudite—or pseudo-erudite—scholar and finally to the practical scientist—an evolution in which a rise in ethical and educational standards was accompanied by a corresponding increase in

popular regard. The more closely the doctor has approached to the high standard of the Hippocratic code the higher have the public esteemed him. Secondly, we have noted how easily decadence can set in, the wisdom of one civilization being lost for centuries and preserved, if at all, by what appears to be a mere chance. Can we be so certain this will never happen again? It nearly happened in 1940, as the rapid decline of medicine in Germany under the false ideology and tyranny of the Nazis proves.

Thirdly, we have marked how some of the most enlightened civilizations—for instance the Chinese, Indian, Egyptian and even the Greek in the end—have been marred by confining the provision of medical care to certain sections of the population. You may say that such a thing is impossible in the England of to-day, but have we, for instance, treated the uninsured black-coated workers and lower-paid sections of the professional classes fairly in this respect?

Fourthly, we have noticed how during the most advanced and humane phases of many civilizations, the State has appointed medical officers to care for the poor, to guard against epidemics, and to protect, and even prescribe, the food and drink of the people—in other words to practise preventive medicine. We are proud—and justly so, I believe—of our country's record as a pioneer in this kind of work, but progress must be continuous if we wish to avoid decay and that progress cannot be left to public health officials or enthusiastic laymen: it depends for its success on the active, intelligent, day-to-day co-operation of the general practitioner.

Lastly, we have been struck by the way in which decadence in medicine has coincided with over-specialization on insufficient knowledge. Can we feel so safe against the re-currence of this danger? You may say that modern medicine is truly scientific and that a high degree of specialization is necessary if we are to reap the benefits of new dis-coveries and expert procedures. There is much truth in this contention, but even in these enlightened days we know of manufacturers launching new remedies on the market based on new discoveries but backed by extravagant claims not justified by the scientific evidence available, remedies snatched at by harassed practitioners in the hope that they may benefit patients whom nothing seems to cure or even alleviate; we know that there are specialists whose outlook is so cramped that they tend too often to attribute their patients' ailments to some unusual condition in their own sphere. The only sure defence against over-specialization is, I believe, to give the general practitioner a dominant share in the care of the patient, and to fit him for this important position in the State, we must see to it that he is rightly educated. All of us who have been medical students know the fascination of the study of fully developed disease, the care of dangerous illness, and the dramatic appeal of difficult operations. But the prevention of disease and the achieve-ment and preservation of perfect health, both physical and mental, also have a compelling appeal if presented by teachers who have the right outlook on health and disease, and I refuse to believe that the medical student of to-day, the brother of the radiolocation opera-tor who accurately fixes the unseen aircraft at an incredible distance; and of the anti-aircraft gunner who hits a target he cannot even see—I cannot believe that the medical student in his turn is incapable of feeling the fascination and satisfaction of detecting the first glimmering of ill-health in his patient and defeating it, of adjusting his patient to the environment with the same pride and accuracy with which the skilled member of a R.A.F. maintenance crew adjusts his "kite".

I have heard it maintained that the general practitioner should concern himself solely with so-called "clinical medicine", by which I suppose is meant the treatment of developed disease—in other words he is to turn a blind eye to the opening stable door, waiting until the horse is loose to start chasing it. Surely this is entirely contrary to all the traditions of our profession—and indeed contrary to common sense. No one, I think, expects the general practitioner to be an expert on environmental hygiene, though he should understand its principles; or to be an epidemiologist, though he should certainly be familiar with the ways in which infectious diseases are transmitted. But if he is to do his duty as the guardian of the patient's health he must know three things; first his patient's heredity and environment, including his home circumstances and conditions of employment—in short all the factors which may result in a deviation from perfect mental and physical health; second, his medical history and present condi-tion; and third, but by no means least, all the agents, including not merely methods of treatment, but also all the public and private organizations, which can be invoked to restore him to his normal or a condition better than this.

During the last two centuries the good general practitioner has established himself in the esteem and affection of his patients as a guide, philosopher and friend, though recently certain social tendencies and the growth of specialization have, as I have already pointed out, tended to some extent to undermine this position, to the detriment of the people's health. We must not only re-establish him as the trusted confidant and

guardian of the patient *and of the family*, but we must strengthen his position in every possible way, placing in his hand all the weapons that modern science and State organization have provided.

I am convinced that the general practitioner is to-day presented with a wonderful opportunity—which, if neglected, may never recur—of occupying a key position in medicine and in the State, and from that position exercising an incalculable influence for good on the health and happiness of his fellow countrymen, thereby ensuring to himself, a life of absorbing interest and abiding satisfaction in the greatest of all professions.

Let us promote the *private* practitioner to be a *general* practitioner, a real general marshalling all the forces of the State and voluntary organizations for the capture of health.

> Come, then, dear friend on whom so oft we've leant
> In sickness sore and anguish of the soul.
> You for whose aid we ne'er in vain have sent
> Help us, before disease can take its toll.
> Show us the way to win life's greatest wealth
> Body and mind attuned in perfect health.

[I am greatly indebted to Dr. Charles Singer for his invaluable advice on the historical portion of this address.]

REFERENCES

1 FRAZER, J. (1941) The Golden Bough (abridged edition in one vol.), London.
2 WONG, K. C. and WU, L. T. (1932) History of Chinese Medicine, Tientsin.
3 NEUBURGER, M. (1910) History of Medicine (translation by Playfair), London.
4 WITHINGTON, E. T. (1894) Medical History from the Earliest Times, London.
5 BRIM, C. J. (1936) Medicine in the Bible, New York.
6 PUSCHMANN, T. (1891) A History of Medical Education from the most remote to the most recent times (translation by E. H. Hare), London.
7 FARRINGTON, B. (1941) *Bristol med.-chir. J.*, 58, 45.
8 RIESMAN, D. (1935) The Story of Medicine in the Middle Ages, New York.
9 SIMON, J. (1890) English Sanitary Institutions, London.
10 POWER, D'A. (1940) *Brit. med. J.* (ii), 437.
11 NEWMAN, G. (1932) The Rise of Preventive Medicine, London.
12 FRASER, T. (1939) *Brit. med. J.* (ii), 209.
13 JASTROW, M. (1913) The Medicine of the Babylonians and Assyrians. *Proc. Roy. Soc. Med.*, 7, 109, Sect. History of Medicine.
14 BREASTED, J. H. (1930) The Edwin Smith Surgical Papyrus, Chicago.
15 SINGER, C. and D. (1924) " The Origin of the Medical School of Salerno, the First University. An Attempted Reconstruction " in Essays on the History of Medicine, presented to Prof. Karl Sudhoff, Edited by C. Singer and H. E. Sigerist, Zurich and London, p. 121.
16 SINGER, C. (1929) " Salerno " Encycl. Brit., 14th Ed.

Section of Experimental Medicine and Therapeutics

(Formerly called Section of Therapeutics and Pharmacology)

President—R. D. LAWRENCE, M.D.

[*November 9, 1943*]

DISCUSSION ON PENICILLIN

Professor A. Fleming: Penicillin is the name which I gave in 1929 to an antibacterial substance produced by a mould of the genus Penicillium. Of the hundreds of varieties of penicillia only one, *P. notatum*, is known to produce penicillin. A penicillium starts as a spore of perhaps 1/200 of a millimetre in diameter. When this germinates one or more threadlike processes grow out which branch and form a felted mass—it may be several inches across. In a short time special hyphæ grow up into the air and these develop fruiting bodies with myriads of fresh spores. These fruiting bodies in different moulds have different appearances which are used by mycologists in the botanical classification of such organisms. The genus Penicillium derives its name from the resemblance of its fruiting body to a pencil or brush.

These mould spores are very common in the air and normally the bacteriologist keeps his culture plates well covered to prevent mould spores or other organisms contaminating them. It happened that in 1928 I was engaged in a bacteriological research on staphylococci and when for examination purposes I had to remove the covers of my culture plates a mould spore drifted on to a plate. After a time it revealed itself by developing into a colony about half an inch across. It was no new thing for a bacteriologist to find that a mould had grown on a culture plate which had lain on the bench for a week, but the strange thing in this particular case was that the bacterial colonies in the neighbourhood of the mould appeared to be fading away. What had a week before been vigorous staphylococcus colonies were now faint shadows of their former selves. I might have merely discarded the contaminated culture plate as I had done contaminated plates before, but fortunately my previous research work on antiseptics and on naturally occurring antibacterial substances caused me to take special notice of the apparent antibacterial action of the mould. I, therefore, made subcultures of the mould and investigated the properties of the antibacterial substance, and all the penicillin made in this country hitherto has been made from descendants of the original colony which contaminated my plate.

I found that it was readily diffusible in agar and was a strong inhibitor of some microbes, notably the pyogenic cocci, while it had no inhibitory action on others such as the typhoid-coli group, the influenza-pertussis group, plague and others. I mention that it was readily diffusible in agar. That may seem unimportant, but I am not sure this is so, as all chemicals which have proved successful chemotherapeutic agents have been very diffusible, while some others which did not so diffuse but which otherwise were very active on bacteria failed clinically.

Then I found that while the crude culture fluid in which the mould had grown was strongly antibacterial it was non-toxic to animals and to human leucocytes. This was in 1929, when there was no thought of the sulphonamides, and all the antiseptics which I had previously tested had been more poisonous to human leucocytes than they were to bacteria. The blood by itself, by virtue of the living leucocytes, kills off most of the infecting bacteria, but as the concentration of antiseptic is increased so the bacterial growth is increased until a point is reached where all the bacteria which were inoculated grow out. This is due to the greater lethal action of the antiseptic on the leucocytes than on the bacteria.

Penicillin was the first antiseptic I had tested which (even in its crude form) inhibited the growth of bacteria in blood while it had no inhibitory action on the leucocytes. It was this especially which made me say in my first paper on the subject that it might be an efficient antiseptic for application to, or injection into, areas infected with sensitive microbes.

The crude penicillin was, however, very unstable and was too weak and too crude for injection. Early attempts at concentration were not very successful, and after a few tentative trials its clinical use was not pursued, although it has been in use in the laboratory since 1929 for differential culture. Its resuscitation as a chemotherapeutic is due to the brilliant work of Florey and his colleagues at Oxford who succeeded in concentrating

and purifying the active principle of the crude culture fluid to such an extent that it could be administered to patients by intravenous or intramuscular injection in sufficient quantity to exercise its extraordinary antibacterial action.

I will not go into clinical results—they will be given by subsequent speakers—except to say that we have treated a considerable number of cases by penicillin administered generally or locally, and that our experience has been at least as happy as has that of the other British and American workers.
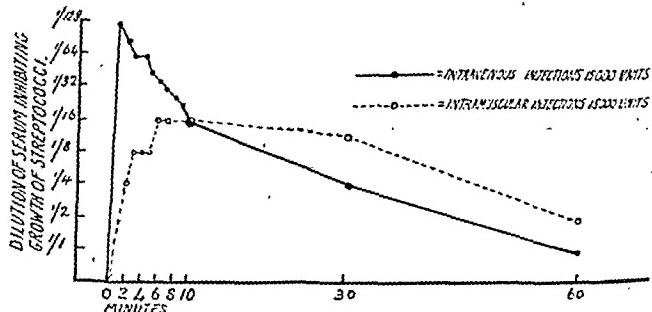
FIG. 1.—Bacteriostatic power of patient's serum after (i) intravenous and (ii) intramuscular injections of 15,000 units of penicillin.
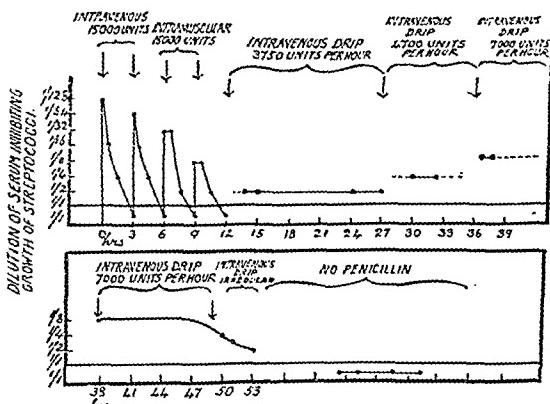
FIG. 2.—Bacteriostatic power of patient's serum after intravenous and intramuscular injections and a continuous intravenous drip at different rates.
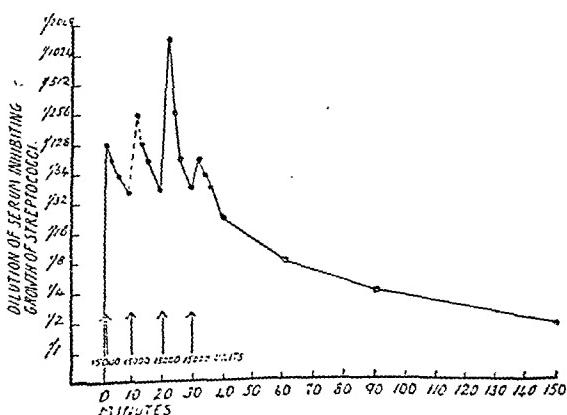
FIG. 3.—Bacteriostatic power of patient's serum after repeated intravenous injections of penicillin at short intervals.

I would like, however, to draw attention to certain points in connexion with penicillin treatment. In the first place it should not be used to treat an infection by a microbe which is not sensitive to the drug. It is very easy to test whether a microbe is sensitive and this should be done in every case.

The method which I had previously used for testing the sensitivity of organisms to lysozyme, the sulphonamides, and other chemicals, is probably the simplest. A strip of medium is cut from a culture plate and the bacteria to be tested are streaked across the plate at right angles to the gutter thus formed. The gutter is then filled with melted agar containing penicillin. After incubation the bacteria are found to be inhibited for a greater or less distance from the penicillin according to their sensitivity.

Then it is desirable to make tests of the bacteriostatic power of the blood to see whether sufficient of the drug is being administered to give to the blood an enhanced bacteriostatic power. I want to show you some charts; the first shows the bacteriostatic power of the blood serum after an intravenous and an intramuscular injection. Immediately after the intravenous injection, as might be expected, there is an enormous increase of the bacteriostatic power, but this falls very rapidly so that in two hours there is no detectable bacteriostasis (fig. 1).

With the intramuscular injection there is a very definite rise in two minutes illustrating the rapidity with which the drug gets into the blood. The blood level never reaches anything like the height that it does one minute after the intravenous injection, but after ten minutes the blood level is as high with intramuscular as with intravenous injection of the same dose and after that the drop is slower.

The next chart (fig. 2) shows the results of intravenous and intramuscular injection and of an intravenous drip.

With the injections after five minutes there is a high level of penicillin in the serum—higher with intravenous than with intramuscular injection—and a rapid drop so that no bacteriostatic power is discernible in undiluted serum three hours after injection. With the intravenous drip there is a constant level of bacteriostatic power merely depending on the amount of penicillin infused.

There may be doubts as to which method of administration is the best, but all of them are effective—that has been proved beyond doubt.

In another patient an attempt was made to obtain a cumulative effect by repeating intravenous injections at intervals of ten minutes, so that the second and subsequent injections were made when the blood level was still considerable. The next chart (fig. 3) shows the bacteriostatic power of the serum.

It will be seen that there was a cumulative effect for the first three doses so that one minute after the third dose the blood serum could be diluted over 1,000 times and still inhibit hæmolytic streptococci. Nothing like this result has ever been obtained with any other drug. It will also be seen that two hours after, even after another injection, the bacteriostatic power had fallen to a low level. Urine collected in this interval contained an enormous amount of penicillin so that even when diluted 20,000 times it inhibited the growth of staphylococci. What this means can be somewhat appreciated when we remember that this is about the same dilution at which acriflavine loses its bacteriostatic power and 50 times greater than the extreme dilution in which carbolic acid inhibits growth.

Effect of penicillin combined with phagocytosis.—The following experiment seems to be very important. A solution of penicillin was titrated and the indicator was hæmolytic streptococci in blood treated in various ways so that the leucocytes were alive or dead, or the serum was active or inactive.

The results are shown in Table I.

TABLE I.—EFFECT OF PENICILLIN IN BLOOD WITH AND WITHOUT PHAGOCYTIC MIXTURES.

		Phagocytosis		Penicillin dilutions				
			1 1	1/2	1/4	1/8	1/16	Control
Defibrinated blood	= { active leucocytes / active serum	+	0	0	0	+	+	-
Defibrinated blood heated to 50° C.	= { leucocytes killed / active serum	--	0	0	+	+	+	+
Defibrinated blood deleucocyted	= { leucocytes removed / active serum	-	0	0	+	+	+	+
Defibrinated blood + liquoid 1 1000	= { leucocytes killed / inactive serum	-	0	0	+	+	+	+
Washed corpuscles + heated serum	= { active leucocytes / inactive serum	-	0	0	+	+	+	+
Washed corpuscles + unheated serum	= { active leucocytes / active serum	+	0	0	0	+	+	+

It will be seen that whenever active leucocytes and active serum were present together, so that phagocytosis could take place, the apparent titre of the penicillin was higher than when either the leucocytes or the serum was inactive. In the body, therefore, where

phagocytosis is possible it may be that a good clinical result can be obtained even when the amount of penicillin administered is so small that in undiluted serum no bacteriostatic power can be detected.

It may be that the most important use of penicillin is in local treatment by application to or injection into an infected area or cavity. It is of some importance, especially at present when the supply is short, to determine where possible how long the injected penicillin remains in sufficient concentration to be effective, so as to know how often to repeat the application. Figure 4 is a culture plate which bears on this. Penicillin was injected

FIG. 4.—Culture plate showing the bacteriostatic effect of *penicillin contained in pus.*

Pus was aspirated from an axillary abscess 24 hours after the injection of 500 units of penicillin in 0·5 c.c. The upper half of the plate was planted with staphylococci and then discs of agar were removed and the holes thus made were filled with pus. There was sufficient penicillin in the pus to inhibit growth of the staphylococci through a wide area.

On the lower half the same pus was planted with a wire in the usual way. At A there was a large quantity of pus and here there is no growth, but at B where the organisms had been streaked away from the pus many colonies of staphylococcus appear.

into an axillary abscess, and after twenty-four hours pus from the abscess was aspirated. This was placed in two cups in an agar plate which had been planted with staphylococcus. It will be seen that there was sufficient penicillin in the pus to diffuse out into the agar and inhibit the staphylococcal growth for a distance of 13 mm. On the lower half of the plate the pus was spread. Where it was thick there was no growth owing to the amount of penicillin in the pus, but where it was streaked very thinly staphylococci grew out. Thus we had a pus which had in it sufficient penicillin to be strongly bacteriostatic and which yet contained plenty of living staphylococci.

This illustrates the fact that the action of penicillin is bacteriostatic rather than bactericidal. Thus with penicillin, as with the sulphonamides, the actual destruction of the infecting bacteria has to be done by the body cells. It seems to follow, therefore, that the best results will be obtained in patients who have the highest degree of immunity and that, although in most patients brilliantly successful results will be obtained by penicillin alone, we must not forget that there will be some cases where immunological methods will help, just as in the case of the sulphonamides.

It gives me pleasure to think that the merits of penicillin were disclosed as the result of *in vitro* laboratory tests, and not as with some other chemicals from testing substance after substance on animals till one was found to work. The discovery of the exact chemical nature of penicillin, and its ultimate synthesis is the goal we must aim at. This may be of vastly greater importance than a mere increase in the production of penicillin, for once the chemists know the formula and have prepared penicillin they will proceed to play tricks with its molecule, as they have with the molecule of sulphanilamide in the last five years, and give us chemicals even more potent and of wider application.

Professor H. W. Florey: I shall begin by emphasizing that the development of penicillin for clinical use has only been made possible by the close collaboration of the team of workers at Oxford. Their work has all been done with Professor Fleming's original strain of *Penicillium notatum*, using culture media based on Professor Raistrick's formula. While the clinical work was done with partially purified material containing from 2% to 15% of penicillin, which was entirely satisfactory for that purpose, highly purified preparations have now been obtained which will prevent the growth of staphylococci and streptococci

at dilutions between 1:50,000,000 and 1:100,000,000, and will produce morphological changes at a dilution of 1:256,000,000. The organisms most sensitive to penicillin are the gonococcus, meningococcus, streptococcus, pneumococcus and staphylococcus, the anthrax bacillus and the Clostridia. Others such as the typhoid bacillus are less sensitive, but may be within the therapeutic range of the more highly purified preparations. The coliform group of organisms and *Proteus* and *B. pyocyaneus* are insensitive, as is unfortunately the tubercle bacillus also.

Professor Florey then outlined the pharmacological properties of penicillin which, determined in the laboratory before clinical trials were undertaken, had established the conditions under which it could be successfully used. He then continued: As its production involves much labour and skill it is essential that every precaution should be taken against loss of potency during storage and manipulation. Penicillin is most stable between pH 5 and pH 7. It is destroyed by acids and alkalis, by boiling, by heavy metals such as copper and lead, by oxidizing agents and by enzymes from many common bacteria, including some air bacteria and some of the coliform group. It appears to be entirely non-toxic to animals and man and it is not inhibited by blood, serum, tissue autolysates or pus. Within wide limits the number of bacteria present has no effect upon its action. It is a very soluble substance and is rapidly absorbed from subcutaneous tissue and muscle. It cannot be given by mouth, as the acid in the stomach inactivates it, nor by rectum as enzymes from the coliform bacilli present in the fæces destroy it. Intravenous or intramuscular injections are suitable means of administration. It is excreted rapidly in the urine, bile and saliva but does not pass freely into the tears, pancreatic juice, or cerebrospinal fluid.

Up to the present time efforts have been directed to finding the minimum effective dose, but this resulted from difficulties of production, not from any toxicity of the penicillin itself. Indeed it appears to be unique in that, given ample supplies, there is no need to worry about the upper limit of dosage. It has been established here, and confirmed in the U.S.A., that staphylococcal and streptococcal septicæmia in man can be cured by the parenteral administration of about 15,000 units every three to four hours. (The unit is an arbitrary standard which was originally adopted in the Laboratory at Oxford for convenience in assay, but which is now in general use in this country and America.) If treatment of such a septicæmia does not cure it can be said with certainty that failure is due to one of three causes—inadequate dosage, the use of an inactive preparation of penicillin, or insensitivity of the organism. It should not be forgotten that organisms can acquire resistance to penicillin and that insensitive strains are found among species usually sensitive. For example, Major Scott Thompson has recently found that about 4% of strains of *Staph. aureus* isolated from wounds in the Middle East were naturally resistant to penicillin.

Local administration is very effective in suitable cases, if certain conditions are fulfilled. There must be adequate access to all infected areas, and a concentration of penicillin sufficient to inhibit bacterial growth must be maintained continuously till the body defences have had time to deal with the bacteria. The development of special surgical methods is often essential in order that these conditions may be fulfilled.

Through the co-operation of the Army, Brigadier Cairns and I have recently been able to visit the Middle East theatre of war and to apply these principles in the treatment of war wounds. It appears that at the present time almost every war wound is potentially infected and it is the current Army practice not to close any wound received at the Forward Base Hospital more than six hours after infliction. Our aim has been by applying penicillin as early as possible to eliminate the bacteria and obtain primary closure and healing.

[Professor Florey then showed a film which he had made in the Middle East showing the technique of penicillin administration to war wounds and some of the results obtained.] At the Forward Base Hospital, after excision of skin edges and dead tissue, the wound is closed, a series of fine rubber tubes to the base of the wound being stitched in place. Penicillin solution is instilled through these twice daily for five days. In successful cases —the great majority—of soft tissue wounds, healing is complete in ten to twelve days. The film also showed some examples of the techniques which had been tried for cleaning wounds already septic and for treating compound fractures. The method of treating fractures, while showing promise, needed further technical development to reach the degree of success obtained with soft tissue wounds.

F/Lt. D. C. Bodenham, R.A.F.V.R.: The treatment of localized infections by direct applications of penicillin has shown the value of this method in certain conditions, in others the response to treatment has been poor.

Some methods of treatment have been evolved during the last eighteen months at a R.A.F. Hospital.

The penicillin, made available by the kindness of Professor H. W. Florey, has been supplied as the calcium salt in powder form. The potency has varied from 6·8 to 160 units per milligram in the different samples.

Daily applications of 4 units per square centimetre have proved effective in eliminating streptococci and staphylococci from infected burns. This dose represents but a fraction of a milligram and it is impracticable to apply such a quantity evenly. Dilution of the powder to a standard potency has been found necessary.

Three preparations have been used to treat different types of wound: (a) Solution in water; (b) emulsion cream; (c) powder. They are prepared in the following manner:

(a) *Solution.*—The calcium salt is readily soluble in water. Standard solutions are used in strengths of 500 and 250 units per cubic centimetre.

(b) *Emulsion cream.*—A sterilizable emulsion base is made from:

Lanette wax SX.	33%
Vaseline	33%
Water	to 100%

The wax, vaseline and water are mixed together at 140° F. and readily form an emulsion. Wide-mouthed screw-capped glass jars are half filled with the base and sterilized in the autoclave at 15 lb. pressure for twenty minutes. The jars are shaken as they cool to prevent separation of the emulsion into vaseline and water. When at room temperature a solution of penicillin, strength 500 units per cubic centimetre is stirred into the base. A final strength of 100 units per gram is found the most useful.

This oil in water emulsion, with water forming the continuous phase, is a thick yellow cream of good spreading consistency. It is readily miscible in all proportions with water, adheres to a moist surface and can be removed by the action of water alone.

(c) *Powder.*—Penicillin is mixed with a sterilizable and neutral powder. Sulphanilamide has been chosen for this purpose. Light magnesium oxide added to the sulphanilamide prevents caking after it has been autoclaved.

Sulphanilamide powder	95%
Light magnesium oxide	5%

The two powders are mixed and sterilized in the autoclave at a pressure of 5 lb. for fifteen minutes. Penicillin is added when cold and the mixture completed by shaking. This produces a good powder which may be used in an insufflator if necessary.

Principles of treatment.—A successful result will follow only if the following conditions are observed:

(1) The primary invading organisms must be sensitive to the action of penicillin. Gram-positive cocci are usually sensitive even if they are resistant to the sulphonamides. Secondary invaders, B. proteus and the coliforms, particularly B. pyocyaneus are clinically insensitive to penicillin.

(2) The penicillin must reach all parts of the wound in an effective concentration throughout treatment.

(3) The removal by surgical methods of other factors which prevent healing, such as: (a) Rigid and fibrotic walls of a cavity preventing collapse; (b) reduction in the blood supply to the part following fibrosis; (c) presence of dead tissue.

Professor Fleming has pointed out that success in treatment depends as much on the natural defence processes of the tissues as on the bacteriostatic power of the penicillin.

CLASSIFICATION OF WOUNDS AND THEIR TREATMENT

Six types of wound commonly occur.

Type I: Surface Wounds—Burns.—The infection is superficial and is accessible to applications of penicillin in the form of cream or powder. They respond well to treatment.

The cream, in a strength of 100 units per gram, is thinly applied with a sterile wooden spatula. If the wound is large time is saved by applying the cream to the dressings: the prepared side of the dressings is then laid on the wound surface. Daily applications are necessary if there is profuse discharge, this tends to dilute and wash away the penicillin. Otherwise applications every forty-eight hours are adequate. Streptococci and staphylococci disappear from swab cultures four to five days from the commencement of treatment.

The sulphonamide powder mixture, strength 1,000 units per gram, applied every twenty-four hours as a light frosting is effective, though the results have not been as consistent as those following the use of the cream. In either case a dose of 4 units per square centimetre is aimed at. This powder is innocuous to skin grafts and may be applied under grafts at the time of operation.

The elimination of coccal infection from burns and surface wounds hastens healing and allows earlier skin grafting with greater prospect of success than would otherwise be the case.

Type II: Gutter wounds.—Such wounds may follow infection of clean operation cases or bomb or road accidents. Recent cases respond well to powder or cream preparations. These wounds are often complicated by deep pockets which must be searched for and treated (see below).

Success depends on an exact knowledge of the position of the wound. The information gained from repeated swab cultures must be the guide to subsequent treatment.

In simple cases a cream of strength 250 units per gram has been successful. A wound with bone involvement and complicated by deep pockets 10 × 2 × 1½ in. in size, required 10,000 units daily divided between powder applications to the wound surface and a solution strength 500 units per cubic centimetre injected through a fine catheter into the pockets. Such treatment, if successful, allows of early secondary suture or skin grafting.

In late cases, where the walls are fibrotic and rigid, operative treatment is necessary. Penicillin alone is unsuccessful.

Type III: Sinuses.—Recent sinuses are effectively treated by the injection of a solution of penicillin of strength 250 units per cubic centimetre. The solution is injected through a thin rubber tube or catheter passed to the limit of the sinus. Sufficient is used to fill the sinus and injections are repeated every four hours without disturbing the tube.

Operative treatment is necessary in late cases where the walls are rigid and avascular.

Type IV: Dependant cavities.—These are treated by injections of a solution strength 100 to 250 units per cubic centimetre. As a guide to the amount of solution required, an amount equal to 10% of the volume of the cavity is injected every four hours. The tube is left undisturbed in the cavity during the intervals. By reason of their dependancy the solution is easily maintained in contact with all parts of the wound. In early cases the response is good, the infection is eliminated and the cavity heals. Operative measures to collapse or cauterize the cavity are necessary in late cases.

Type V: Inverted cavities.—Local penicillin treatment without surgery has been disappointing in these cases. Failure is due to the technical difficulty of maintaining the penicillin in contact with the entire surface of the cavity throughout treatment. A few successes have been gained where the stoma can be plugged around the tube and they are treated as Type IV. In other cases operative procedures are necessary.

Type VI: Complicated cavities.—This group includes multilocular abscess cavities and complex joint cavities such as the knee. In these it is *impossible for the penicillin to reach all parts of the wound all the time.*

Local treatment alone has been most disappointing. Two cases of acute staphylococcal arthritis of the knee each received 10,000 units daily by needle puncture for eight days. The temperature did not return to normal nor were successive sterile swabs obtained. Such cases should either be treated on established surgical principles with local penicillin as an additional weapon or should receive large doses of penicillin parenterally.

Incidence of secondary infection with coliform organisms.—Secondary infection of war wounds with *Bacillus pyocyaneus* whilst under treatment with penicillin has occurred in some cases treated during the last eighteen months. It has been observed that solutions of penicillin strength 250 units per cubic centimetre can easily be contaminated with the living organisms. This is one source of infection.

Storage of penicillin.—Dry powder preparations often retain their full potency for one to two months when stored in the dark at room temperature. As this, however, is not constant it is probably better to store them in a refrigerator. Solutions and cream preparations will retain their potency for three to four weeks when stored at 3° C. Contamination of these preparations with *B. pyocyaneus* is associated with a rapid deterioration in potency. This is probably due to the production by the pyocyaneus of a substance which causes a breakdown of the penicillin. This may be similar to the penicillinase described by Abraham and Chain (*Nature*, 1940, 146, 837).

Colonel **Elliott C. Cutler,** U.S.A.M.C.: *The value of penicillin in preventing serious spreading of infection when the Clostridia are present in the wound.* In a study now going on with our 8th Air Force every alternate casualty receives penicillin. This varies from 10,000-20,000 units of penicillin instilled into the wound by spraying after complete debridement has been carried out. The penicillin is in the strength of 500 units of penicillin to 1 c.c. of normal salt solution. Following this initial wound treatment with penicillin, the penicillin is given parenterally, 10,000 units every three hours for three days. If serious infection arises this dose is doubled.

Amongst the group of individuals treated recently there have occurred three serious infections with Clostridia. This is perhaps indicative that either we are not using a proper dosage, or that penicillin acts differently in the human being than in the experimental animal subjected to clostridial infection or that our method of getting penicillin to the area infected is faulty.

One of these cases was a British motor cyclist with compound fracture of the right femur and of the right tibia; he had also a thrombosis of the femoral artery at the level of the fracture of the femur. The other two were airmen; one had extensive muscular damage to both thighs, destruction of a segment of the right sciatic nerve, and a compound comminuted fracture of the right femur; the other had compound comminuted fractures of the right tibia in the upper third.

Some methods of treatment have been evolved during the last eighteen months at a R.A.F. Hospital.

The penicillin, made available by the kindness of Professor H. W. Florey, has been supplied as the calcium salt in powder form. The potency has varied from 6·8 to 160 units per milligram in the different samples.

Daily applications of 4 units per square centimetre have proved effective in eliminating streptococci and staphylococci from infected burns. This dose represents but a fraction of a milligram and it is impracticable to apply such a quantity evenly. Dilution of the powder to a standard potency has been found necessary.

Three preparations have been used to treat different types of wound: (a) Solution in water; (b) emulsion cream; (c) powder. They are prepared in the following manner:

(a) *Solution.*—The calcium salt is readily soluble in water. Standard solutions are used in strengths of 500 and 250 units per cubic centimetre.

(b) *Emulsion cream.*—A sterilizable emulsion base is made from:

Lanette wax SX.	...	...	...	33%
Vaseline	...	...	...	33%
Water	...	...	...	to 100%

The wax, vaseline and water are mixed together at 140° F. and readily form an emulsion. Wide-mouthed screw-capped glass jars are half filled with the base and sterilized in the autoclave at 15 lb. pressure for twenty minutes. The jars are shaken as they cool to prevent separation of the emulsion into vaseline and water. When at room temperature a solution of penicillin, strength 500 units per cubic centimetre is stirred into the base. A final strength of 100 units per gram is found the most useful.

This oil in water emulsion, with water forming the continuous phase, is a thick yellow cream of good spreading consistency. It is readily miscible in all proportions with water, adheres to a moist surface and can be removed by the action of water alone.

(c) *Powder.*—Penicillin is mixed with a sterilizable and neutral powder. Sulphanilamide has been chosen for this purpose. Light magnesium oxide added to the sulphanilamide prevents caking after it has been autoclaved.

Sulphanilamide powder	...	...	...	95%
Light magnesium oxide	...	...	...	5%

The two powders are mixed and sterilized in the autoclave at a pressure of 5 lb. for fifteen minutes. Penicillin is added when cold and the mixture completed by shaking. This produces a good powder which may be used in an insufflator if necessary.

Principles of treatment.—A successful result will follow only if the following conditions are observed:

(1) The primary invading organisms must be sensitive to the action of penicillin. Gram-positive cocci are usually sensitive even if they are resistant to the sulphonamides. Secondary invaders, *B. proteus* and the coliforms, particularly *B. pyocyaneus* are clinically insensitive to penicillin.

(2) The penicillin must reach all parts of the wound in an effective concentration throughout treatment.

(3) The removal by surgical methods of other factors which prevent healing, such as: (a) Rigid and fibrotic walls of a cavity preventing collapse; (b) reduction in the blood supply to the part following fibrosis; (c) presence of dead tissue.

Professor Fleming has pointed out that success in treatment depends as much on the natural defence processes of the tissues as on the bacteriostatic power of the penicillin.

CLASSIFICATION OF WOUNDS AND THEIR TREATMENT

Six types of wound commonly occur.

Type I: Surface Wounds—Burns.—The infection is superficial and is accessible to applications of penicillin in the form of cream or powder. They respond well to treatment.

The cream, in a strength of 100 units per gram, is thinly applied with a sterile wooden spatula. If the wound is large time is saved by applying the cream to the dressings; the prepared side of the dressings is then laid on the wound surface. Daily applications are necessary if there is profuse discharge, this tends to dilute and wash away the penicillin. Otherwise applications every forty-eight hours are adequate. Streptococci and staphylococci disappear from swab cultures four to five days from the commencement of treatment.

The sulphonamide powder mixture, strength 1,000 units per gram, applied every twenty-four hours as a light frosting is effective, though the results have not been as consistent as those following the use of the cream. In either case a dose of 4 units per square centimetre is aimed at. This powder is innocuous to skin grafts and may be applied under grafts at the time of operation.

The elimination of coccal infection from burns and surface wounds hastens healing and allows earlier skin grafting with greater prospect of success than would otherwise be the case.

loosely applied. The intramuscular dosage of penicillin was increased to 20,000 units every three hours. Transfusions amounting to 1,500 c.c. of blood were given and treatment with anti-gas gangrene serum was begun. 100,000 units of the serum were given intravenously. The serum consisted of 50,000 units against *Cl. welchii* and 50,000 units against *Cl. septicum*. The day following operation some devitalization of the proximal muscles was discovered. This was slight in extent and the involved muscle was excised under pentothal anæsthesia. 20,000 units of penicillin were instilled in the wound on wet gauzes. 200,000 additional units of anti-gas gangrene serum were given subsequently and the patient was transfused repeatedly.

Cultures from the tissue excised at the operation immediately following injury showed no growth. Cultures of the wound at the time infection was discovered showed organisms morphologically compatible with *Cl. welchii*. Further identification is being carried out. (Stormy fermentation in iron milk.)

During the period of penicillin treatment the patient received a total of 60,000 units in the wound and 1,050,000 units parenterally. The activity of the penicillin in the patient's serum was tested against the standard Florey staphylococcus on October 15. A bactericidal effect was shown up to two hours and there was strong bacteriostasis three hours after the dose of penicillin.

CASE III.—G. M., aged 20.

On October 14, 1943, while on an operational mission over Germany the patient was severely wounded on the posterior aspects of both thighs by a rocket shell which exploded near the plane. The greater part of the musculature of the posterior right thigh was blasted away, a segment of the sciatic nerve was destroyed, and there was a compound comminuted fracture of the middle third of the femur. The large vessels, however, were intact. Damage to the posterior surface of the left thigh was extensive and involved the destruction of a considerable part of the hamstring muscles; the left sciatic nerve and the large vessels were not disturbed and there was no fracture.

The patient arrived at the hospital exsanguinated and in profound shock. With large infusions of plasma and the transfusion of 1,500 c.c. of whole blood he rallied sufficiently to permit operation. There was, however, a necessary time interval of twelve hours between injury and operation.

Operation.—The operation consisted of a thorough debridement of the right thigh wound including the compound fracture. The wound of the left thigh was also debrided but on account of the poor condition of the patient, the debridement was incomplete. Penicillin was sprayed and instilled into both wounds, each receiving 10,000 units.

The fracture was treated by suspension and traction by means of a Kirschner wire which had been passed through the upper tibia before the debridement was started.

The patient appeared to be doing well until his third post-operative day when an X-ray taken to determine the position of the bone fragments revealed the presence of gas in the tissues. Upon inspection of the wound, necrotic muscle and a small amount of gas were found. Smears taken showed a great number of Gram-positive rods with subterminal spores. Cultures subsequently yielded Gram-positive cocci and Gram-negative rods, in addition to the spore-bearing rods.

With this confirmation of the clinical diagnosis of gas gangrene amputation was carried out approximately at the site of fracture, though the bone was cut across at a slightly higher level. The open stump was sprayed with 20,000 units of penicillin and the parenteral dosage was increased from the standard 10,000 units every three hours to 20,000 units every three hours.

After operation, gas gangrene antitoxin for *Cl. welchii* and *septicum* was given in daily doses of 100,000 units, a total 400,000 units being given.

On the second day after amputation additional necrotic muscle appeared on the end of the stump and was cut away.

Although the debridement of the wound of the left thigh was far from complete and clostridia were cultured from its surface no clinical manifestations of a gangrenous process developed on this side. The patient has made satisfactory progress and recovery is in prospect. During the period of penicillin therapy the patient received a total of 40,000 units in the wounds and 1,020,000 units parenterally; his serum was definitely bacteriostatic for the standard Florey staphylococcus throughout the course of treatment. (Stormy fermentation in iron milk.)

CONCLUSIONS

The administration of penicillin in the three cases described did not prevent the development of gas gangrene.

The effect of penicillin therapy on the course of the disease is difficult to estimate.

All of the three patients are recovering, two following mid-thigh amputations, and one following excision of the involved group of muscles.

Mr. R. Vaughan Hudson: It is my privilege to report upon the cases under the care of the Middlesex Hospital Penicillin Research Committee, and to acknowledge their permission and the utility of the notes of Dr. Parkes, our research registrar.

Thirty-three cases were selected for treatment because they were penicillin-sensitive. An equal number of cases were fully investigated but not treated either because they were penicillin-insensitive or more suitably treated by other means.

The great majority were treated by the systemic route in combination with local application. A few by local application alone.

The cases fall into two main groups, the closed and the open. In the closed the portal

In the two cases with fractured femurs and gas gangrene, amputations were done at the fracture levels. In the patient with fractures of the tibia and fibula, infection was confined to the anterior muscles of the leg; these were excised and there was no further spread of the infection. All of the three patients who had clostridial infection are doing well and their recovery seems assured.

CASE I.—D. W., driver (motor cycle), aged 21.
Admitted to hospital September 29, 1943, following a motor cycle accident in which he sustained a compound fracture of the mid-shaft of the right femur and a compound comminuted fracture of the right tibia. The right fibula was not fractured.
There was extensive damage to the soft parts of the right thigh. The upper fragment of the femur projected anteriorly several inches through the skin, and the posterior fragment pointed posteriorly. The ends of the fragments were separated by about 5 in. The patient was in considerable shock, and his red blood count was 2,700,000 with 58% hæmoglobin. The right thigh and leg below the femoral fracture were cold and no pulsation could be detected in the posterior tibial or the dorsalis pedis arteries.
After receiving 1,200 c.c. of plasma and 500 c.c. of whole blood, the patient was operated upon, the interval between injury and operation being three hours.
Operation.—Both wounds were carefully debrided and 15,000 units of penicillin were sprayed and instilled into the femoral wound and 5,000 units in the tibial wound. Cultures from the wounds taken after debridement showed no growth.
Following the operation the patient was given 10,000 units of penicillin intramuscularly every three hours.
The third post-operative day, there were signs of gas gangrene but cultures were negative.
The fourth day after operation, the cultures of tissues had grown a *Clostridium* and a Gram-negative bacillus. By this time the clinical evidence of gas gangrene was unmistakable and an amputation was done at the site of the femoral fracture. The amputation stump was sprayed with 10,000 units of penicillin. The parenteral dose had been increased on the day before operation to 20,000 units every three hours instead of the original 10,000 units.
The adductor group of muscles which were gangrenous were excised on October 5. After the excision another 10,000 units of penicillin were put in the wound. Once the diagnosis of gas gangrene had been established gas gangrene antitoxin was administered in doses of 67,500 units to 155,000 units until a total of 457,500 units had been given. The antitoxins used were for *Clostridium welchii* and *Cl. septicum*, and the spread of the clostridial infection appears to have been arrested.
The administration of penicillin was discontinued on October 7, at which time the patient had received a total of 40,000 units in the wound and 1,080,000 units parenterally.
During the period of penicillin administration the patient's serum exhibited active bacteriostatic properties against the standard Florey strain of staphylococcus.

CASE II.—Sgt. W. H. E., aged 24.
This patient sustained compound comminuted fractures of the left tibia and fibula on an operational mission over enemy territory at 23,000 ft. on October 14, 1943. He thinks that the injury occurred at 1500 hours and that the missile was a 20 mm. shell.
He was admitted to hospital at 2020 hours October 14 in profound shock. After 1,400 c.c. of plasma and 1,000 c.c. of blood were administered operation was performed at 0300 hours October 15.
Operation.—Under local anæsthesia a Kirschner wire was inserted through the left os calcis. Under pentothal anæsthesia the skin of the left leg was prepared with soap, water and ether. The tibia and fibula had been fractured at the junction of the upper and middle thirds. Both were badly comminuted but there was relatively little loss of bone. The actual defect in the soft parts was approximately 5½ in. long and 4½ in. across. There was marked tissue loss involving the tibialis anticus, peroneus profundus and longus muscles, and considerable overlying skin. Tissue maceration was extensive but little gross dirt or clothing was carried into the wound. A narrow margin of damaged skin was cut away and much devitalized and fragmented muscle excised. All of the muscles remaining bled from their surfaces but there was no contractility. A hanging flap of skin was sutured back in place but the wound was not changed from an open to a closed one. Approximately 2,000 c.c. of saline were used for irrigation and 10,000 units of penicillin (500 units per 1 c.c. of normal saline) were either sprayed or poured into the wound over which vaseline gauze was loosely placed. The leg was put on a Braun splint and traction applied. The fracture was satisfactorily reduced. His condition was good and the dorsalis pedis and posterior tibial pulses were strong.
Another 1,000 c.c. of blood were given during operation. Despite this his blood-count was 1·7 million the day following operation and another 1,000 c.c. of blood were given.
Immediately following operation he was started on 10,000 units of penicillin intramuscularly every three hours.
The patient did quite well but pallor and low R.B.C. count were disturbing factors. Transfusions were frequently given. Temperature varied between 100° and 102° and pulserate did not rise above 110. The dressing became stained reddish yellow but not until October 17 (approximately fifty-two hours following operation) was an offensive odour noted. The wound was dressed and there was clinical evidence of gas gangrene. He was taken to the operating room and under pentothal anæsthesia all devitalized tissue was removed. The flap of skin referred to above was green-brown in colour. The proximal muscles looked normal. The distal portions of the divided muscles as far down as their tendinous portions had undergone varying stages of damage from complete autolysis to simple ischæmia. There were numerous gas bubbles present and some slight œdema of the subcutaneous tissues. By degrees the skin on the anterior surface was opened down to the ankle. Every bit of involved muscle was removed. This meant excision of the distal portions of the tibialis anticus and the two peronei. After excision of the muscles, 20,000 units of penicillin were placed in the wound and vaseline gauze

(1) Of 34 cases with a sinus leading to infected bone, 14 were cured, 13 improved, and 7 unaffected. In all but 3 cases the infection was of more than one month's duration. Where it seemed unlikely that the penicillin administered could reach the more remote parts of the infection, results were poor, and the presence of sequestra was usually, but not always, an unfavourable factor.

(2) Of 44 cases with infections of soft tissues, 28 were cured, 10 improved, and 6 unaffected. Most satisfactory results were obtained in recent infections, and the accessibility of the tissues involved was again an important factor.

(3) In 9 cases of sycosis barbæ, 8 of which were of more than two years' duration, and selected because they had failed to respond to the ordinary methods of treatment, 7 were apparently cured after the application of penicillin in lanette wax cream for two or three weeks. In three of these cases only one side of the face was at first treated, and in all the treated side rapidly improved. In 3 cases a relapse occurred in from one to five weeks, but these have responded to a second course of treatment. In the remaining 2 cases no improvement was observed, and although the infecting organism developed some degree of penicillin resistance, there also appeared to be sensitivity to the lanette wax and vaseline base, and other methods of application are now being tried. 4 cases of impetigo have also been treated with penicillin with outstanding success.

In the first two groups the application of penicillin was sometimes preceded by surgical intervention, but in most of these surgery alone had previously proved ineffective. The calcium salt of penicillin was used in solution (500 to 1,000 units per cubic centimetre of water) or in lanette wax cream (200 to 400 units per gram), and in a few cases as the powder diluted with sulphanilamide (1,000 units per gram). In all cases the sensitivity to penicillin of the infecting organism and the effects of treatment on the bacteriology of the wound, were studied under the direction of Professor Garrod.

Lieut.-Colonel J. S. Jeffrey, R.A.M.C.: There is an interesting complication of penicillin treatment—the problem of Gram-negative pus. With adequate dosage of penicillin there is no difficulty in disposing of the Gram-positive invaders of a war wound, but the Gram-negative organisms such as *B. pyocyaneus, Proteus* and *B. coli* are insensitive to the drug, and their pus collects in any dead space in the wound, particularly in the large spaces of a compound fracture. The pus is thin and salmon-pink in colour and may run freely out of the wound in quite alarming fashion. However, it seems to do little harm except for delaying healing slightly, for it disappears spontaneously in a few days and the wound remains quiescent and uninflamed. The important thing is not to be alarmed at its appearance, nor to be tempted to release the stitches of a sutured wound. If a dead space is unavoidable it is advisable not to suture the wound completely, but to suture the ends of the wound as a support for granulations and to leave a natural drainage channel in the centre for the escape of the Gram-negative pus. We made the mistake, in our first fifty cases in the Middle East, of suturing so tight as to dam up the pus, which was of little consequence in the soft tissue wounds but led to slow healing of some fracture wounds.

As regards the treatment of gas gangrene, I believe that penicillin is the chemotherapeutic agent of choice since it inhibits the Clostridia more surely than do the sulphonamides. Given parenterally, it should prevent multiplication of the infecting organisms and the spread of infection, but will not prevent absorption of toxin from gangrenous muscle to which the blood-stream cannot gain access. For this reason it is auxiliary to, and in no way supersedes, the other two essentials of treatment, viz. radical surgery and large doses of gas gangrene antitoxin. Penicillin may, however, increase the number of cases in which local excision of gangrenous tissue is sufficient, and reduce the incidence of amputation.

Dr. M. E. Florey: Following the earliest clinical trials carried out by Dr. Charles Fletcher, a further investigation into the clinical application of penicillin was made during 1942 and 1943 on upwards of 300 cases.

Throughout the investigation an effort was made to correlate bacteriological findings with clinical progress. Treatment was not considered complete till either the original infecting organisms could no longer be cultivated or the lesion had healed, which sometimes happened before negative swabs had been obtained. Clinically the types of infections treated were:

(1) Generalized infections. (2) Chronic sinuses. (3) Skin infections. (4) Infections of the eyes and eyelids. (5) Abscesses. (6) Empyemata. (7) Cases of arthritis. (8) Cases of acute mastoiditis. (9) Acute infections of the hand. (10) A miscellaneous group.

of entry is fractional, the organism is usually single and tissue damage is due to that organism and has not been complicated by previous trauma.

The open type are of two categories: (1) where the breach of surface is relatively small and has been due to either spontaneous rupture upon the surface or to a limited surgical exposure; (2) where the portal of entry is large such as in gun-shot wounds, compound fractures and burns. In this group the damage to the circulation and death of tissue by trauma has already complicated the issue and facilitated the early invasion by mixed organisms. With one exception, we have not been enabled to treat cases of this second sub-category.

In the evaluation of the results the stage of the disease from its onset may be classified under three headings: (1) Stage of early invasion and cellular death; (2) stage of partial mobilization of a tissue barrier with molecular necrosis; (3) stage of full mobilization and massive necrosis.

The application of a specific remedy such as penicillin, sufficiently early may alter the whole picture.

However it must not be presupposed that because a remedy is successful in Stage 3 it is of necessity of value in Stage 1.

We have learnt so much from the use of the sulphonamides that the clinical properties of penicillin and its superiority can be appreciated by utilizing this standard of comparison.

From the sulphonamides one has learnt that the organism must be sensitive to the particular sulphonamide employed. Their use in the face of an insensitive organism is actually harmful to the patient. The maintenance of their bacteriostatic action is finally limited by the toxicity of the substance with subsequent inhibition of the hepato-renal function and destruction of the white cells. Penicillin appears to be non-toxic, a supreme advantage. A percentage of apparently favourable organisms are in fact sulphonamide-resistant. Under-dosage, incorrect apposition, all tend to harden the organisms and render them insensitive. A high percentage of these sulphonamide-fast organisms are penicillin-sensitive. Penicillin has reinforced our knowledge that a wound can be sterilized but that it will not heal if the blood supply or local metabolism is insufficient. Alternatively, in the face of a good blood supply and the lowering of the bacterial count a wound will heal in spite of the fact that it is not completely sterile.

The contents of abscess cavities are lethal to the patient and drainage by minimal interference and reintroduction of an effective agent are important, for apposition must be maintained and the penicillin not permitted to run away before its action is complete.

Even if penicillin is applied to the surface of a slough it will fail to penetrate its deep undersurface, and we have learnt the supreme value of this drug in that when applied by the systemic route it will break the stubborn adhesion between the dead tissue and the living. It has proved to us that this adhesion is due to continual activity of living organisms. If they are inhibited by the systemic application this slough will rapidly separate, become fragmented by tissue proteolytic action and converted into thin fluid.

The dosage necessary to do this lies somewhere between 100,000 units and 300,000 units by three-hourly intramuscular injections, according to the stage of the infection. Whether this will enable us to deal with death of bone in its early stages by the tissues defences alone safely and permanently is still a matter of conjecture, though it may be possible.

The stability of the sulphonamides has been a most useful property, particularly in the fact that they can be administered by mouth.

The solubility of penicillin is in one way an asset, as it can be applied locally as a calcium salt or can be rapidly dissolved in sterile saline and applied as a wet dressing or through catheters as in the Carrel and Dakin technique.

The impossibility at the moment of administering penicillin by mouth is its greatest disadvantage.

The intramuscular route has given us the most constant results. Repeated puncture every three hours has been a great burden to the sick patient. Its impurities render venous thrombosis at the site of injection frequent and local reaction marked, and like the sulphonamides it is extremely irritating to peripheral nervous tissue.

Dr. Parkes has found that the use of novocain reduces the irritation and the discomfort of the injection considerably, and does not affect the efficiency of penicillin.

Professor Ronald V. Christie (*Abridged*): I am speaking for a group of physicians and surgeons at Hill End Hospital, where, during the past six months, we have treated 117 cases with penicillin, 104 of them by local application and 13 by systemic administration. In the cases treated systemically the results have borne out what has already been said, and the administration of penicillin by a drip into the bone-marrow has been tried in three cases with some success. Of the cases treated locally I will only mention those included in the following three groups:

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[*November* 23, 1943]

DISCUSSION ON THE STATE OF NUTRITION IN ENEMY-OCCUPIED EUROPE

Lord Horder, Chairman of the Advisory Medical Council of the
Famine Relief Committee, introduced the speakers

Colonel W. Vignal (French Army Medical Corps): *The health situation in France.*—That health conditions in France are intimately connected with food supplies is shown not only by reports from private sources, but also by an official and confidential report by the present Minister of Agriculture, Max Bonnafous, at Vichy. This report was meant for the German authorities only.

The basic meat ration is only 90 g. (3¼ oz.) a week, 105 g. (3¾ oz.) for hard and 210 g. (7½ oz.) for very hard workers. The daily basic ration allowed to each of the population of France is equivalent to 884·4 calories. Even with the extra quantities distributed from time to time in certain big centres, it barely reaches 1,100 calories.

In 1917-18 the Germans' ration averaged 1,600 calories: according to them this was the cause of emaciation, loss of strength, low blood-pressure, bradycardia and psychological breakdown, and they called the state a semi-famine. The French population now cannot get more than 1,100 calories, except for a favoured few who can add at the most 100 to 300 more. The vast majority get less than 1,500 calories, and their diet is ill-balanced at that, being deficient in fats, proteins and sugar.

Ill-health among adults.—The lack of protective foods, such as animal fats, butter, cheese and eggs, causes a general weakening with consequent increase in such diseases as tuberculosis, which is increasing alarmingly. According to Dr. Grasset, the Minister of Health at Vichy, 35,000 of the 4,963,000 inhabitants of the Seine Department are afflicted with tuberculosis, and the proportion of young women among the patients is alarmingly high. For instance, in 1938 the numbers of new cases for each 100,000 head of population was 141, in 1941, 161, and in 1942, 176. The death-rate from tuberculosis per 100,000 has risen correspondingly.

In a paper read to the Académie de Médecine on September 2, 1941, Marcel Moine reported the following facts from a single department, that of the Oise. The number of sputum analyses with positive results for every thousand patients has risen by 44·5 to 47·3%. In another department, according to Étienne Berthet, the number of tuberculosis patients detected has risen by one-third. He says that an ill-balanced diet is perhaps more responsible for this outbreak than undernourishment due to insufficient total intake.

In 1941 the Germans sent back to France a large number of prisoners of war, all tuberculous. Apart from the dying, all were borderline cases for treatment. The majority had bilateral, and many extrapulmonary lesions. Of the artificial pneumothorax cases, 70% needed division of adhesions and 15% needed further operation. This is a result of too long delay in treatment. These patients were discharged from the Army too soon, about six weeks after repatriation—and most of them could not be kept under treatment, as they were impatient to go home. They are

JAN.—MED. 1

The majority of these infections were due to staphylococci. A large number were due to streptococci, or staphylococci and streptococci. Some were caused by pneumococci, gonococci or actinomyces, and from a few only species of organisms insensitive to penicillin could be cultivated.

The results obtained from treatment of these infections may be summed up as follows: In 14 no response to treatment was noted; in 41 improvement resulted; in over 250 complete recovery from the infection occurred.

These results appear particularly striking in view of the fact that they include the experimental cases on which the dosage for systemic administration was worked out, various routes of administration were tried and concentrations, vehicles and techniques for local application were worked out experimentally. The criteria used for assessing the effectiveness of penicillin treatment were as follows:

In chronic cases, in cases that had been resistant to other forms of treatment and in moribund cases, it was considered sufficient evidence if, concurrently with penicillin treatment, the infecting organisms disappeared from the lesions and the onset of recovery was observed clinically. In acute cases different criteria had to be used. In these, either the results of the new technique were compared with the old, as in the mastoid series, or a concurrent series of control cases was closely watched and compared with those treated with penicillin, as in the infections of the hand.

The investigation on infections of the hand comprised 100 control and 100 treated cases. The conditions before treatment and the operative procedures were the same in each series. Controls were given sulphonamides by mouth when considered necessary. Penicillin-treated cases received only local applications of the drug.

Bi-weekly bacteriological examinations revealed the fact that all but 6 control cases remained infected for over a week. In 75% no single swab was free of infecting organisms during the whole course of treatment from first incision to complete epithelialization. In the penicillin-treated cases bacterial growth had disappeared or diminished considerably in all but 9 cases during the first week and in 75% had disappeared before healing. (The bacteriological work was carried out by Dr. Robert Williams.)

From a clinical point of view the earliest difference in the penicillin-treated cases was the rapid relief of pain, which ceased soon after operation. Other points were: Scanty production and absence of pus; rapid reduction in swelling of surrounding parts; a reduction in healing time to about half to two-thirds that of the control cases.

The most striking result, however, was the rapid restoration of function and the completeness with which function was regained, as compared with the controls.

Major J. N. Robinson, U.S.A.M.C.: *Penicillin therapy in the treatment of sulfa-resistant gonorrhœa.*—95 cases of sulfa-resistant gonorrhœa and 3 cases of gonorrhœal arthritis were treated with penicillin in U.S. army hospitals in the E.T.O. The cases chosen were resistant to sulfathiazole and sulfadiazene or a combination of both. The average duration of the disease was five weeks before beginning penicillin therapy. Anterior urethritis, posterior urethritis, acute prostatitis and acute epididymitis and arthritis were included in the types of cases treated.

92 cases received 10,000 units of penicillin given intramuscularly every hour for 10 doses—a total of 100,000 units. One case with gonorrhœal arthritis received a total dose of 200,000 units. Two other cases received penicillin in a continuous infusion given over a period of several days. 15,000 units were placed in each litre of saline.

94 of the 95 cases of sulfa-resistant gonorrhœa were considered apparently cured after penicillin therapy. The one failure received two courses of penicillin (100,000 units each course) and still had a urethral discharge which was positive for gonorrhœa one week after treatment.

One of the 3 cases of gonorrhœal arthritis was cured and received 200,000 units of penicillin. The other two cases received only 100,000 units which may explain their failure.

Some observations noted in the 94 successfully treated cases were that the urethral discharge persisted for an average of three days after penicillin therapy. In practically all these cases the smears and cultures were negative for gonorrhœa the following day. The cases of prostatitis and epididymitis were asymptomatic at the end of seven days.

There were no toxic manifestations from penicillin injections in any of our cases.

The first 30 cases followed over one month have shown no evidence of a urethral discharge and weekly urine analyses have been normal. Cultures and smears of prostatic fluid one month after treatment have all been negative for gonorrhœa.

is big, tense, and resonant; growth is hindered and there are many psychomotor troubles · which may be referred to spasmophilia.

According to Ribadeau-Dumas the diet, consisting almost exclusively of crude vegetable matter, causes an excessive elimination of calcium, which in any case is deficient in the intake. An excessive quantity of cellulose, especially ortho-cellulose, in the diet causes food to pass too rapidly through the digestive tract and so leads to an abnormal elimination of proteins as well as to the disturbance in the balance of chlorides and water.

Emphasis must be laid on the psychological disturbances which appear among young persons. The number of neurotic children suffering chiefly from kleptomania, pathological lying, enuresis, epilepsy and sexual perversion, has increased disquietingly.

Deaths among the newly born.—Many children born prematurely at 8 months have the blood characteristics of a fœtus of 6 months. In 1942, 21% of the children in the big towns had between 3,000,000 and 4,000,000 red cells instead of 5,000,000, and this year the percentage is increasing. More than half the newly born weigh less than 3 kg. Many miscarriages are due to undernourishment during pregnancy, and some may be due to eating bread made with spurred rye. Before the war rye was mostly given to cattle, but it is now used in bread. Women are unable to nurse their children: many parturient women show signs of osteomalacia.

Professor Charles Richet, of Paris, was imprisoned for writing in the *Bulletin de l'Ordre des Médecins* of March 1943: "I assert that in the towns 10,000,000 French persons are suffering from hunger and 2,000,000 of these are likely to die from hunger either directly, or indirectly through some infectious disease."

BIBLIOGRAPHY

(*Some Entries are Incomplete Owing to War Circumstances*)

AMEUILLE and SCHWEISGUTH (1943) " Tuberculose pulmonaire à évolution rapide chez un carencé," Société médicale des Hôpitaux de Paris, *Bull. méd., Paris, 57*, No. 18, p. 283.
BALTHAZARD, Prof. (1943) Presidential Address, Académie de Médecine, January 5.
BERTHET, ETIENNE (1941) " Note sur la recrudescence de la tuberculose," Société d'Etudes scientifiques sur la Tuberculose, June 28.
BONNAFOUS, MAX (1943) Report to the Reich Supply Minister, March, 1943, *Les Cahiers Français*, No. 44, June 15. London.
BOURGEOIS, P., VIE, J., and BELLIN, A. (1943) " Les tuberculoses de famine étudiées dans les hôpitaux psychiatriques de la Seine," *Bull. méd., Paris, 57*, 270.
CAYLA, A., LAMMAY, C., and BOULANGER-PILET, G. (1943) " La diminution du poids chez les écoliers de la ville de Paris en 1941-1942," *Pr. méd.,* No. 54, p. 774.
FEIL, ANDRE (1943) " Considération sur le poids actuel des travailleurs," Académie de Médecine, *Bull. méd., Paris, 57*, No. 14, p. 220.
FOREL, O. (1943) " La sous-alimentation en France," *Rev. méd. Suisse rom.,* No. 4 p. xlvii.
GIRARD, JEAN, LOUYOT, PIERRE, and VERAIN, MARCEL (1943) " Les effets des carences alimentaires sur certains éléments du sang," Académie de Médecine, January 27.
HERMANN, H., and VIAL, J. (1943) " Sur la présence de substances constrictives dans le pain," Académie de Médecine, *Bull. méd., Paris, 57*, No. 13, p. 203.
LEROY (1943) " Rapport sur les examens pondéraux des jeunes," Académie de Médecine, August 5.
MOINE, MARCEL (1941) " Un danger qui grandit : la tuberculose," Académie de Médecine, September 2.
MOREL, FRANCOIS (1943) " Acquisitions nouvelles sur quelques aperçus de laboratoire en fonction des conditions présentes," *Bull. méd., Paris, 57*, No. 19, p. 197.
RIBADEAU-DUMAS, L. (1943). " Quelques conséquences de l'alimentation actuelle chez l'enfant," Académie de Médecine, *Bull. méd., Paris, 57*, No. 18, p. 203.
RICHET, CHARLES (1943) " Sur la limitation temporaire des exercices physiques," Académie de Médecine, January 27.
TANON, L., and DALIMIER, P. (1943) " La pratique des grands sports," Académie de Médecine, September 2.

Dr. A. P. Cawadias (President of the Greek Red Cross in Foreign Countries): *The History of Greek famine during the present war.*

The prodromic stage of the famine (Undernourishment in Greece from the beginning of the war to the occupation of Greece, end of May 1941).—Greece is a country that does not produce much food and has therefore to rely to a considerable extent on importation of its food supplies from abroad. This importation is made exclusively by sea, because Greece is virtually an island. Overland transport is extremely difficult, and the one-track railway by means of which Greece communicates with the mainland of Europe is absolutely insufficient for any important traffic. In times of peace, in wheat alone an average of 40,000 tons per month was imported.

The conditions of the food supply deteriorated rapidly when Greece herself entered the war; first, because the shipping problem did not allow for a sufficient quantity of food to reach the country; second, because the local production fell sharply as a result of the general mobilization.

The first phase of the famine (May 1941 to end October 1941).—Upon the occupation

JAN.—MED. 2

therefore a permanent source of infection. Besides these, an increasing number of workmen are returning to France after only a few months in Germany to die of acute tuberculosis. Before the war France was well supplied with sanatoria and hospital beds, but she is now largely deprived of them by enemy requisition. There is also a great deficiency of surgical and medical supplies. Therefore the patient has to wait for six to eight months after detection before he can be admitted to a tuberculosis centre.

Acute forms of the bronchopneumonia type of tuberculosis are very frequent and the extension of the lesions is very rapid and often bilateral. O. Forel states that as a rule only three months elapse between the first symptoms and death. These forms have been observed in patients who have wasted rapidly without showing any signs in a systematic X-ray investigation. He also states that in May 1942 fewer deaths occurred. The reason seems to be that the less resistant have been eliminated; nevertheless the situation remains most distressing. According to the latest information in 1941 there were 150,000 deaths against 234,000 in 1942. Tuberculosis is not the only cause of distress. Many deaths which occur with no apparent cause are thought to be partly due to a deficiency in vitamins, especially vitamin B, and partly to deficiency of sugar. There is no doubt that the situation is most tragic in towns. More and more frequently men collapse in the factory, office or street; many die on being brought home, from no apparent cause other than extreme weakness.

Among the working classes emaciation is the lot of everyone, and in some workers the decrease in weight is catastrophic. Owing to this universal weakness of workers the number of accidents at work has greatly increased. In a metal works near Lyons during the first five months of 1941, 61 working days were lost through accidents; during the corresponding month of 1942 the loss was 147 days. The signs of undernourishment were a progressive asthenia, incapacity for any exertion, and attacks of dizziness. Other symptoms were retro-orbital or temporal headache, copious night sweats, and great susceptibility to cold. The mental syndrome included loss of memory, apathy followed by irritability, auditory hallucinations, and deep depression. Clinically there was low blood-pressure, and loss of weight varying from 12 to 15 kg. in a few months, with hypoglycæmia and ascorbia. The blood-count showed leucopenia in 32% and leucocytosis in 22%. In 58% the mononuclears were above 35%, in 55% the eosinophils were above 4, and in six subjects they were above 10%.

According to Girard, Louyot and Verain the troubles observed in these subjects were said to be due not only to undernourishment but also, and probably mainly, to an ill-balanced diet causing defective assimilation of vitamins, animal proteins, fats and calcium, and thus a chronic dietary toxæmia.

The impairment of function of the vegetative nervous system was probably due to avitaminosis B; but the great difficulty of finding food and its bad distribution have also brought about, especially in towns, a general vindictive and grasping mentality which may cause social upheavals.

Defective hygiene due to the great scarcity of soap, hot water and other facilities for cleanliness is responsible for a great increase in skin infections. Delousing and disinfecting posts have been installed in Paris and the suburbs. Fortunately there were only a few cases of typhus, which had been quickly dealt with.

Ill-health among children.—The situation among children is perhaps even more alarming. O. Forel, a Swiss physician, investigated 45,060 children in towns and industrial centres in the Unoccupied France of 1942. His figures show that of children 3 years old 22% had lost weight and 51% were stationary; between 7 and 12 years 30% had lost weight; and 13 and 17 years 16% of boys and 24% of girls had lost weight.

Cayla and his colleagues point out in the *Presse Médicale* of December 19, 1942, that loss of weight among children of the Paris schools is most severe between 14 and 18, especially among the girls and may be as much as 5 kg. Next in severity is the loss in the age-group between 10 and 12; the younger children are less affected, probably because their parents stint themselves to feed them.

Tuberculosis is on the increase among schoolchildren and in certain centres the death-rate has risen by 30%. It afflicts especially children of 15 and over.

The frequency and severity of rickets is due to shortage of calcium, because milk is scarce and very poor in quality.

A syndrome very often seen among children nowadays is characterized by epigastric tension, abnormal volumes of flatus, enormous fæces and often enuresis. The abdomen

in the world was solicited and the International Red Cross made an appeal to all belligerents to help to stop this terrible Greek famine. The necessary safe guarantees were given by the Axis powers.

The Greek Red Cross in Foreign Countries was instituted with its centre in London. In January 1942, as Red Cross guarantee was given for the relief sent to Greece, the British and United States Governments took the matter in hand. A first food ship was sent to Greece through the action of the British Government and arrived in Greece in April 1942. About this time medicines were also sent. Since then the British and United States Governments directed the relief effected through the Red Cross organizations and a special Swedish-Swiss Commission. In fact, the Swedish Government and the Swedish Red Cross, as well as the Swiss Government and Red Cross, devoted themselves to the relief of Greek famine.

The third period of famine (period of lull) May 1942 to December 1942.—The arrival of that restricted relief caused a period of lull in the terrible period of mortality and morbidity.

This lull was, however, interrupted by certain epidemics among which dysenteric diseases were prominent and an epidemic of typhus, which occurred in Athens, usually immune from such epidemics,-was the danger signal for what was to come.

Food distributions in Greece during that period, according to our information, were as follows:

1942 Month			Kind of food			Per week	Per week Calories	Per day Calories
June	...	...	Olive oil	...	...	2 oz.	555	79
			Sugar	...	...	2½ oz.	317	45
		.	Raisins	...	...	2½ oz.	234	33
								—157
July			Raisins	...	...	2½ oz.	234	33
			Rice	...	...	1 1/3 oz.	130 .	19
								— 52
August	...	...	Sugar	...	...	2½ oz.	317	45
								— 45
September	...		—			No distribution whatever took place		
November	...		Bread	...	...	2 lb. 14½ oz.	2,618	374
			Flour	...	...	2½ oz.	240	34
		.	Pastes	...	...	2½ oz.	268	38
			Sugar	...	...	3½ oz.	300	43
			Porridge	...	...	10 1/3 oz.	1,067	152
			Dry beans	...	...	10 1/3 oz.	868	124
								—765
December	...		Bread	...	...	2 lb. 14½ oz.	2,618	374
			Porridge	...	...	10 1/3 oz.	1,020	146
			Flour	...	...	10 1/3 oz.	957	137
			Sugar	...	...	3½ oz.	300	43
								—700

During that period, although we have no precise statistics, it seems that deaths from pure starvation diminished and also that general mortality diminished approximately to normal figures. However, as a danger signal morbidity increased, bearing principally on malaria, tuberculosis and severe deficiency diseases.

The fourth or actual-period of famine, period of instability (from beginning of 1943). —Although during 1943, thanks to the relief, the food rations in Greece improved and a certain lull was marked in the mortality, although not in the morbidity, this period can be characterized as Period of Instability and there have been lately symptoms of recrudescence. This is easily understood: The food rations distributed to-day in Greece following the relief, are insufficient, and this is shown by the following comparison taken from the figures published in the book "Starvation Over Europe" compiled by the Institute of Jewish Affairs in America. In this it is shown that whereas the Germans obtain 94% of their normally required calories, the other nations in Occupied Europe obtain less—thus:

Czechs	...	...	...	84%	Norwegians	...	...	59%
Dutch	...	...	...	81%	French	...	...	55%
Poles	...	72%	partly	61%	Greeks	...	...	29%
Belgians	...	...	...	67%				

During summer, on account of the possibility of finding some vegetables and of the good conditions of external temperature, the mortality was not very high, although the

of Greece, the population after its superhuman struggle was in a state of great exhaustion. The armies of occupation consumed the meagre food supplies available and the food ships that would have brought new consignments from abroad were stopped. Populous centres could not get supplies even from the rural areas, because the invasion took a terrible toll of the country itself.

Even fish disappeared from the markets, when small craft were forbidden to leave the shore for fear they might be assisting Greeks, Australian and British soldiers to escape. Already these first months were terrible, although no one could visualize the tragedy which was in store. It was summer, and the Greeks eat very frugally in the summer. Some vegetables could be found in the country districts and there were some scanty stores, allowing the development of the black market, which took enormous proportions.

The official rations were by the middle of August 1941 limited to bread and sugar and amounted to 3 oz. of sugar per week and 2½ oz. of bread per day. The scarcity of milk and milk products became intense because most cattle was slaughtered to fill the immediate needs. The remaining milk-yielding animals, badly nourished because of lack of fodder, gave very little milk.

The general mortality increased by 200% and mortality from tuberculosis also increased about 200%. The condition of the population was appalling.

Toward the end of that period (October 1941) when the first food relief ship arrived from Turkey, the editor of the Turkish newspaper *Vatan* wrote:

> " What I saw in Greece exceeds a hundred times anything that has been written about her plight. It seemed to me as if I had entered hell. I spoke to a person whose clothes hung loosely on him. He had lost half his weight. For five days he and his wife had tasted no food. The thirty grams of bread received as their daily ration they gave to their small children. When one ship's crew went ashore they were surrounded by hundreds of people crying out: 'Give us at least a crumb of bread, we are dying of hunger.' German guards dispersed the crowds. Walking through the town we were overcome with horror. The people we met looked like skeletons."

The second or tragic period of the famine (from the beginning of November 1941 to the end of March 1942).—The official ration at that time consisted of about 1 oz. of bread per day made of seeds, and this was not always forthcoming.

Communal kitchens established in Athens and Piraeus were feeding 50,000 people, i.e. three-quarters of the population. They could give only about 400/500 calories. The well-to-do people, who were too proud to be fed in communal kitchens, had a very poor menu, which according to a report of Mr. Sulzberger, an eye witness. correspondent of the *New York Times*, consisted in Athens of unsugared camomile tea and two slices of bread for breakfast. For lunch, gruel of unsugared wheat with oil and cabbage; for supper, the same with chick-pea coffee. Milk, of course, was practically non-existent and the official ration for babies was ½ oz. of rice per week.

A report of the Save the Children International Union, dated March 1942, states:

> "For eleven months no condensed or powdered milk, which were the main baby food, have been imported. ... Even greater danger threatens babies who are not brought to the clinics and it is now common, alas, to see in the streets of Athens, mothers carrying babies in a condition of athrepsia, and sometimes already dead. ... Many orphans or abandoned children of all ages are found wandering in the streets, near canteens or restaurants, dirty, starving, pale and thin, a sight recalling Dante. They stop at nothing to find a bit to eat; searching among the refuse or fighting the dogs for something edible."

People were dying from starvation in such high numbers and the life of the whole country was so much distorted that no precise statistics could be kept. *The Times* according to a message from Istanbul reported 320,000 deaths from August 1941 to March 1942, i.e. more than ten times the normal rate. The Greek Prime Minister in London in an official statement to the Press said that 2,500 deaths per day occurred during certain months in Athens and Piraeus alone. Epidemics started at the same time, particularly diphtheria and typhus. Tuberculosis spread tremendously but no official statements are available. Tuberculous individuals, of course, could not survive.

The relief during that period was directed with great effectiveness and self-sacrifice by the personnel of the Greek Red Cross in Greece. (It should be noted that the Greek Red Cross is a very important organization in Greece.) The help of all Red Crosses

Rickets was found rarely in towns, but mostly in rural districts where Moslems lived. Sometimes in Slovenia, as well as in Croatia, Banat, Bachka, and Srem, because the children were kept too much indoors. Tuberculosis was spread throughout the whole country. While in the regions which had surplus food the most important cause of tuberculosis was bad housing in the self-supporting ' and less productive areas malnutrition as well as bad housing was responsible. The mortality rate from tuberculosis, was about 30,000 people per year, in peacetime 70,000 children out of 450,000 born every year died before reaching 12 months.

The medical services of the country, and Government action, introduced several measures, to solve the problems of nutrition.

In Enemy-Occupied Yugoslavia.—There is a constant lack of food for many reasons:

(1) The enemy took all stores of food, belonging to the Yugoslav Army, and State, at the beginning of the occupation. By introducing occupational marks, they bought everything they could. When the peasants realized that they could not buy anything, they started sabotage, by introducing a black-market and destroying food which might have gone into enemy hands. Already in 1941 the stores of food were finished and the concern of the people was how they should live until next year's harvest.

(2) The army of occupation (about 250,000) had to be fed.

(3) The harvests of 1942, and 1943 were minimal, for many reasons:

(*a*) Lack of labour: About 140,000 prisoners of war (137,282 on September 15, 1943) were taken to the enemy countries; about 150,000 were taken to different concentration camps; 250,000 people were sent to work in Germany; about 250,000 people are under arms (about 35,000 with General Nedich, and about 200,000 with Pavelich). About one million of the population were massacred, or killed in battle. Many people have joined the guerrilla fighters. More than 200,000 people were deported abroad. Those who are working on the land now under occupation, worked in the same way before the war, with the exception of a few townspeople; (*b*) Shortage of draught animals; (*c*) Sabotage; (*d*) The decrease of cereal-sown areas, to make room for other products, by order of the enemy; (*e*) Continuous guerrilla warfare; (*f*) Transfer of population by force from one area to another. (There are in Serbia about 300,000 refugees from other parts of the country, and about 200,000 in Croatia.)

Our information is not complete enough to make an accurate survey of the position, but taking into consideration the reports coming from the country, we can assume that the average caloric value of the food is about 50% of normal. There is in the country, not only malnutrition, but also famine. All the big towns suffer from malnutrition, and famine. All passive, i.e., unproductive country regions, where malnutrition was combated by the import of foods from the surplus regions, now suffer from famine. This is mainly because of the guerrilla fighting, which has lasted for more than two years, particularly in Montenegro, Sanjak, Bosnia, Herzegovina, and Dalmatia, as well as in Serbia and Slovenia.

All the consequences of malnutrition in peacetime are increasing enormously from day to day. Tuberculosis and children's diseases now cause a greatly increased mortality rate.

If each Yugoslav inhabitant could be provided daily with a kilogram of wholemeal bread and a spoonful of lard, and if the children could be provided with sufficient quantities of milk, fish oil and other vitamins, the Yugoslav famine could be almost immediately alleviated, and the consequences of malnutrition slowly cured. Two normal pre-war harvests, provided that the transport facilities are adequately restored, will be sufficient to return to the pre-war standard of living.

BIBLIOGRAPHY

LEAGUE OF NATIONS (1939) European Conference on Rural Life. National Monographs drawn up by Governments. Yugoslavia. (Official No. C.169. M.99. 1939. Conf. E.V.R.23.)
SEKULICH, M. (1943) Health—Past, Present and Future. Royal Yugoslav Embassy Information Department, London.
YUGOSLAVIA, MINISTRY OF AGRICULTURE (1937) Statistique agricole annuelle.
YUGOSLAVIA, CENTRAL HYGIENIC INSTITUTE OF MINISTRY OF HEALTH AND SOCIAL WELFARE (1937) Yearbook on national health and activities of the health institutes in 1936. Belgrade.

Professor James Young (Vice Chairman, Advisory Medical Council of the Famine Relief Committee): *Food situation in Belgium.*—Official and non-official evidence, said Professor Young, indicated a serious food shortage in Belgium. He referred especially to an

morbidity continued to rise. Reports from Swedish observers mark a tremendous increase in tuberculosis and point out that in regions in which even last year malaria was 30% it has reached 100%. They speak also of an extensive development of hunger œdema. All these are signs that during this winter, if relief is not intensified, very bad conditions are to be expected.

Dr. Milosh Sekulich: *Yugoslavia.*—The state of nutrition in Yugoslavia can be better understood if a comparison is made with peacetime conditions. There were two main types of diet in Yugoslavia: urban and rural. The first was a meat diet, the second of vegetables. The urban population represented about 20%. The meat diet contained roughly 35 kg. of meat per head per year, the vegetable diet contained roughly 9 kg. of meat. There were, of course, in different regions exceptions to this rule, as well as peculiarities.

From a *caloric point of view*, the urban diet at least was normal. It should be mentioned, for example, that unemployment was very low in peacetime in spite of the fact that about 600,000 peasants went to the towns for seasonal work. Wages paid were used mostly to buy food.

Carbohydrates.—The rural diet contained average number of calories for a normal diet.

The consumption of cereals for bread per year, per head of the population in 1936, totalled 394 kg., in 1937, 379 kg., according to the "European Conference on Rural Life" published by The League of Nations (C. 169 M. 99, 1939. Conf.. E.V.R. 23).

The peasants used also, the other various products: potatoes, haricot beans, peas, lentils, broad beans, cabbage, tomatoes, peppers, onions, &c., which were also used by the town population. The people pickled cabbage, gherkins, peppers, &c., for the winter, in town, as well as country.

Fruits consumed were as much as 100 kg. per person per year. The quantity consumed varied from one region to another. Fruit was eaten mostly in the summer. Sugar was consumed at the rate of 5·5 kg. per head, per year.

Albumins.—The small quantity of meat eaten by the peasants was consumed in the winter mostly, and on festive occasions, but the townspeople consumed meat nearly every day. Milk and dairy produce play a more important part in the peasants' than in the townspeople's diet. In 1937, 130 litres of milk were used per person; which quantity can be taken as an average per year. In 1937, 600,000 tons of albumin was consumed in Yugoslavia, this means 60 g. per person per day.

Fats.—Of all fats, lard was the most used by the population, the quantity being 11 kg. per head, per year. The consumption of the various fats in the country, was 22 kg. per head, per year, or 60 g. per day.

Vitamins and minerals.—The country produced a satisfactory quantity.

Caloric value of the above diet.—Foods consumed by the people, and the average caloric value mentioned above, is higher than a normal person needs, and gives a figure of about one and a quarter million calories per head, per year, or nearly 3,500 per head, per day (Table I).

TABLE I.—FOODS CONSUMED BY THE PEOPLE, AND THEIR CALORIC VALUE IN 1937

	Quantity of food per person per year	Caloric value (rough calculation)	Caloric value of 1 kg. of food
Cereals	379 kg.	730,000	2,000
(about 365 kg. of bread)			
Wheat	124 kg.		
Maize	226 kg.		
Barley	10 kg.		
Rye	11·6 kg.		
Oats, buckwheat, millet spelt ...	7 kg.		
Potatoes	70 kg.	42,000	600
Haricot beans, peas, lentils, broad beans	7 kg.	14,000	600—3,000
	17 kg.	4,165	245
Cabbage	3 kg.	480	160
Tomatoes	2 kg.	—	—
Peppers	4 kg.	1,800	450
Onions		60,000	600 (roughly)
Fruits	100 kg.		
Meat	22 kg.	55,000	1,500—3,600

Section of Comparative Medicine

President—J. T. EDWARDS, M.R.C.V.S.

[*December* 15, 1943]

DISCUSSION ON THE LIMITATION AND USES OF THE COMPARATIVE METHOD OF MEDICINE

I.   The President's Address by Dr. J. T. Edwards, M.R.C.V.S., will be published
later in the PROCEEDINGS.

II.   Animal Ecology and Genetics

Mr. Martin A. C. Hinton, F.R.S. : In order to help the growth and interpretation of ecological knowledge our studies should rest on a comparative basis; our results should be recorded in such a way as to facilitate and ensure comparisons along definite though not too rigid lines.

In order to help the growth and interpretation of ecological knowledge our studies should rest on a comparative basis; our results should be recorded in such a way as to facilitate and ensure comparisons along definite though not.too rigid lines.

There is a more important reason for putting our studies on a strictly comparative basis.' The same animal or the same plant may differ very widely, both in constitution and behaviour, at different ages, in different seasons, in different conditions, or in relation to different life-chains. Thus an annual weed in its young, flowering, and fruiting stages, may represent—from an ecological point of view—three quite different plants, differing in habit and chemistry and in their relations to the surrounding animal life.   Similar though usually more marked differences characterize the various stages of insect development. They are found too in many other animals including such highly specialized and at first sight ecologically uniform types as birds and mammals.   In short any living species may play several distinct parts in the economy of Nature in the course of its career.

Experience of one member of an animal group is usually helpful when we have to deal with another; but no matter how full our experience of the first member may be it does not relieve us of the necessity for studying the second in detail.   The two species though closely allied may present important ecological differences which, if neglected or ignored, may easily lead to the positions of danger.   Let me illustrate this by recalling a little of our experience of rats in this country.   The cases (for there are two species of rat involved) are of great medical interest because of the part played by rats in spreading diseases among men and domestic animals.

The two species of the genus Rattus occurring in Britain are:

(1) *Rattus rattus*.—the "Black Rat", "House Rat", "Ship Rat", "Alexandrine Rat", &c., of popular writers characterized by its light build (weight usually not more than 8 oz.),   large thin ears,   long tail (length   exceeding   that   of   head and body together), and short hind-feet (length from heel, without claw, usually less than 40 mm.).

(2) *Rattus norvegicus*—the "Brown Rat", "Common Rat", "Grey Rat", "Hanover Rat", "Norway Rat", "Sewer Rat", &c. of books; characterized by its heavy build (weight of adults commonly 14 to 17 oz., sometimes much more to 20 or 30 oz.), small thick ears, shorter tail (length usually less than that of head and body), and longer hind-feet (length usually more than 40mm.).

Both species are aliens of Asiatic origin and each has spread with commerce to all parts of the globe; indeed one (or both) now goes down in submarines and up in aircraft. Being rats, the two species rather closely resemble each other in general form; and as the colour of the fur is very variable, varying in each in the same way and to the same degree, the two species are hopelessly confused in the minds of the public. If we pay little or no attention to the colour, the two species are easily distinguished in adult stages of growth—and in younger stages too, when we know them.   Like most other Muridæ these two species show high fecundity; abundance of food, warm shelter, and exposure to sunlight all favouring their rapid multiplication; in our cities litters are produced at all

address given to the Royal Belgian Academy of Medicine by Professor Heymans in December 1942. Professor Heymans was a distinguished physiologist and a Nobel Prize winner. In the preparation of his statement he had had access to official data and had had the collaboration of well-known colleagues. Heymans stated that the average daily requirements of the Belgian people were estimated at 2,480 calories, whilst the actual daily basic ration (October 1942) contained only 1,230 calories, i.e. it was 50% deficient. (During the 1914-18 war the average daily ration contained 2,280 calories thanks to the Hoover Commission, which was responsible for sending to Belgium 100,000 tons of food monthly.) Pregnant and nursing women, infants, adolescents, certain classes of manual workers and invalids were entitled to supplementary rations. Making allowance for these there was serious undernutrition especially in adolescents from 14 to 21 years where, instead of 2,600 calories required for health, the average figure did not exceed 1,300 calories daily, representing a 50% deficiency. The effects of undernourishment were especially marked in densely populated areas where the majority of adults exhibited a loss of weight of from 22 to 33 lb. Even in those who had not lost weight there was often a fall in plasma proteins by 10, 20 or even 50%. Hunger œdema then complicated the picture (report of Brull from Liège). With regard to pregnant women Heymans quoted Professor Brouha of Liège to the effect that in 1941-42 the weight gain during pregnancy was in primiparæ only 81% and in multiparæ only 78% of that obtaining in 1937-38. Heymans pointed to the great increase in tuberculosis as shown by the numbers of supplementary ration cards issued only after strict scrutiny of the patients at the dispensary or sanatorium. In seven months (December 1941 to July 1942) these increased from 69,079 to 88,503. Professor Young said that the above data from Heymans' paper referred to 1942. It was known that the situation had deteriorated since then.

Dr. Izod Bennett (Physician to the Middlesex Hospital) said that as medical men, with knowledge of the science of nutrition, they could lay down laws and rules which were of the utmost importance when the question was raised as to how England and other unoccupied countries could help.

The first rule to be followed was to supply calories rather than vitamins. It had been said that if you looked after the calories, the vitamins would look after themselves, and provided we followed the rule so rightly emphasized by Sir John Orr, and supplied ordinary natural foods the vitamin content would always be adequate.

In many countries starvation had been going on for years already, and Dr. Izod Bennett felt that an extra ration, representing some thousand calories, should be made available to be issued on medical certificate in liberated countries; such ration for special cases should be an "invalid" ration of easily assimilated foods, particularly milk, animal foods and foods of high vitamin content.

It was of high importance to assist those countries who would receive an influx of tens of thousands of their countrymen repatriated from Germany. Amidst these returning refugees would be thousands of cases of contagious tuberculosis and the only practical method by which such cases could be detected and segregated was by the use of miniature mass radiography.

species inhabiting the area and was the species responsible for the terrible outbreaks of plague in mediæval and Stuart times.

Period 2.—From the beginning of the eighteenth century to the beginning of the present century.

This might be called the *norvegicus* or Brown Rat period for during it Britain and western Europe were invaded by this species, which was first brought into the region by ships coming from both the northern and southern ports of Russia. Aided by its size, ferocity, stronger constitution and aquatic habits, it spread over the whole of Britain by the waterways; entered the buildings, mostly through the drains, and passing from cellars to attics it completely ousted *R. rattus* from the mainland in the course of a century. That species, however, still flourished at sea and could be found to the end of the period living in the security of the stronger granaries and warehouses of some of our ports.

Period 3.—The twentieth century, marked by the rebuilding of cities and the return of *R. rattus.*

The changes of this century are best illustrated by what happened in the City of London—although they were paralleled in other of our cities and ports. At the close of the nineteenth century *R. norvegicus* swarmed in the old houses which still lined our principal streets; but naturally the infestation was not equal at all points. Places like eating-houses were heavily infested; for instance, one I knew in Fleet Street was visited each night, as the shop closed, by a drove of rats which came in from the sewer by way of the cellar and kitchen, up the stairs into the shop. Two dogs were kept; each night they killed rats until they were tired; then they went to sleep and the rats enjoyed disputed possession until morning when they retreated to the sewer. Food contamination and damage were on a great scale.

During the present century the rebuilding of central London and the work of rat-proofing basements was taken in hand; a vast improvement in the *norvegicus* position became evident. That rat was gradually banished to the sewers and watercourses, where, of course, it still swarms, and to open places like surface railway stations, goods yards and the older warehouses. So complete was this banishment that the innumerable cases of bad infestation by this species of ordinary buildings in the City known to have occurred round about 1900 had dwindled to three only by the year 1936. Rat-proofing against *R. norvegicus* was thus a complete success and buildings designed to resist its attacks remained free from this pest for many years during which the species still swarmed in neighbouring buildings of the old type and in the drains outside.

But in fighting *R. norvegicus* with such conspicuous success we forgot *R. rattus*. Ever since its eviction from the land in the eighteenth and early nineteenth centuries that species, arriving in practically every ship coming to our ports, had been trying to re-establish itself here. So long as *R. norvegicus* was present in the buildings it could not do this. With that species shut out the position changed. Our new commercial palaces, with their hygienic roof-kitchens and sky-lights connected with one another across the streets by unguarded telephone cables, gave *R. rattus* a new opportunity which it did not miss. A nightly procession of these arboreal rats passed over the roofs and along the telephone cables looking for chances; tell-tale marks on many a stack-pipe and on adjacent window sashes showed in many cases just where and how these rats gained access to some of the buildings. New colonies were founded in brand-new buildings within a few days of occupation. So complete and so speedy was the recovery of *R. rattus* in the City (and in other parts of central London) that by 1936 or 37 of all the thousands of rats caught in the City in the course of the year no fewer than 90% or more were of this species—and this in an area where thirty years previously scarcely a single example of the species could have been obtained.

What the effect of the recent "blitz" has been I do not know; but it has most certainly given us a new chance; so that when we come to rebuild our cities *R. norvegicus* and *R. rattus* must both be borne in mind.

From this wearisome story many morals of medical and economic importance can be drawn. Among the most important are two, namely:

(1) That you cannot forecast the behaviour or capabilities of species No. 2 merely from your experience of species No. 1.

(2) That if you create a vacancy by the elimination of any given species it is your own very difficult business to keep it vacant.

How difficult this may be becomes apparent when we recall the fact that in the genus *Rattus* there are nearly 600 species and subspecies: and in the subfamily, to which this genus belongs, several thousand allied forms. Though some of these are of considerable economic importance, few (apart from the house mouse, with which I have no time to

seasons; gestation lasts three weeks (or a month if the female is still nursing); and the number in a litter is commonly 8, but often many more.

Though both species are of Asiatic origin they come from very different parts of Asia. *R. rattus* is a native of the hot eastern countries, the forests of India and Malaya are probably the true home of the species; *R. norvegicus* is a native of Central Asia, the belt of country between the shores of Lake Baikal and those of the Caspian Sea being apparently its original home. With such different origins it is not surprising to find that the two species differ markedly in constitution, habits and history. *R. rattus* from the hot forests is a climber and gymnast, a delicate creature both in build and constitution; it swarms on ships; but in the cold countries of N.W. Europe it could not get through a single winter without the shelter unwittingly given to it by man. In contrast, *R. norvegicus* from the bleak open country is a digger and swimmer, finding all the shelter it requires in the banks of streams; it is a hard robust animal and in all countries invaded by it, the watercourses from the biggest rivers to the small drains form its highways. Like all murine rodents it is quick to take advantage of the shelter and plenty provided by man; but in a country like Britain it is in no way dependent upon man for shelter. Wherever there is ground suitable for burrowing and water not too far off *R. norvegicus* will flourish quite independently. Food for either species may be anything that comes along, although grain is preferred.

The differences of constitution and habits produce a difference in the attitude towards man shown by the two species in this and similar cold temperate countries, a difference not without medical importance. *R. rattus* is so dependent upon man in these countries that it is forced into close association with him and it seems to have realized here, just as it has long done in the native houses of the East, that man, generally speaking, is so inattentive to his surroundings that he is not greatly to be feared; accordingly this species will run along a moulding just above the heads of the customers in a restaurant, make its nest in some careless bachelor's mattress or settle down in his desk. *R. norvegicus* on the other hand with its sturdier independence remains man-shy; it may swarm in the basements of houses, or on a shop floor as soon as the shop is closed, but it beats a hurried retreat to its burrow or to the adjacent drains as soon as man approaches. This man-shyness of *R. norvegicus*, depending partly on the attitude of man to the rat and partly to the rat's more or less complete independence, is seen in all temperate countries; but in very cold countries, as at Tromsø, Norway, or Tammerfors, Finland, in winter, even *R. norvegicus* will overcome its repugnance to close contact with man, going so far occasionally as to make its home in human beds.

In warm or hot countries the position of the two species is reversed; *R. rattus*, whether it be a native or an introduction, feels at home and so it commonly swarms over the countryside, wherever there are trees and bushes, as well as in any buildings to which it can gain access; but *R. norvegicus* though repeatedly and frequently introduced to hot countries remains for the most part confined to the vicinity of the docks and watercourses.

The facts just described are of great interest to anyone considering the spread of plague. Modern research has tended to show that marmots and ground squirrels, inhabitants of open or alpine wastes in Asia and western N. America, are the prime reservoirs of *Bacillus pestis;* and pneumonic plague may be caught directly from the marmots by the trappers in Northern China and elsewhere and be passed on by them to the general human population of the country. Non-contagious bubonic plague is transmitted to man usually from infected *R. rattus* by the agency of its similarly infected fleas. Now if the primary source of *B. pestis* lies in the blood of a ground squirrel or marmot the question arises: How does that organism pass from the ground squirrel or marmot to *R. rattus?*—for these two mammalian species or groups of species do not come into direct contact and there is hardly a chance of any exchange of parasites between them. The most probable answer, in my opinion, is that the burrowing and water-loving *R. norvegicus* coming, as it does, in frequent contact with the marmots and ground squirrels in N. China and Central Asia, gathers plague from them and passes it from rat to rat down the watercourses to the ports and ships, where the species comes in contact with *R. rattus*, which receives infection to be conveyed in due course in bubonic form by its fleas to man in ports possibly thousands of miles distant from the prime source of infection. This view is perhaps borne out by the experience of the Plague Commission in Bombay where plague rose to a peak firstly in *R. norvegicus*, secondly after a week or two in *R. rattus*, and lastly after a similar interval in man.

The history of the two rats in Britain and western Europe is instructive and it falls into three periods, namely:

Period 1.—Extending from the Crusades down to the beginning of the eighteenth century. This might be called the first Black Rat period; for during it *R. rattus* was the only

problems and slight changes in environment, or opportunity may be met by quick and surprising responses not only by organisms immediately under notice, but by many not previously in the picture. I am sure that crude attempts to exterminate certain species, as by laying strychnine baits throughout vast stretches of country, by scattering thallium-treated grain, or by showering down arsenious oxides from the sky, are not sound procedures at all; they may be justified in certain emergencies for a time; but if they became part of an established practice I am sure we should get and deserve sharp punishment in due course from Nature for our presumption.

Animal Genetics

Captain **Hans Grüneberg**, Royal Army Medical Corps: I prefer to speak about the "Uses and Limitations" rather than about the "Limitations and Uses" of the study of inherited diseases in animals for medical science, and I propose to start this survey by a general consideration of the circumstances which make the study of inherited diseases in animals such a powerful tool for ætiological research.

(1) *"Pure" diseases.*—The current classification of human diseases has in the main been evolved by a process of dichotomy and an example will make this clear. The presence or absence of glucose in the urine divides, in a very rough fashion, the diabetics from the non-diabetics; by a refinement of method (blood sugar curve) we can unmask certain diabetics who fail to excrete glucose; similarly, we can segregate certain types of glycosuria by the fact that they do not react to insulin. In general, the present state of the classification of human diseases is a reflection of the clinical and laboratory methods at our disposal; we can thus never be certain whether a given disease is homogeneous ætiologically, or whether a new technique, diagnostic or therapeutic, will prove it to be a mixture of two similar, but ætiologically different, conditions. Sooner or later we shall reach the last fork of the dichotomy, but there is no way of telling whether this has already happened in any particular instance, and it is safe to say that it has not happened everywhere. Clinical material is thus liable to be heterogeneous, and many inconsistencies are no doubt due to this fact. Inherited diseases in animals, on the other hand, are not defined in successive stages by a process of dichotomy. They come into being as gene mutations, suddenly, clearly delineated, like Athene from the head of Zeus. Their genetical (= ætiological) homogeneity can easily be established by a genetical analysis; and if similar material is obtained from different sources, a cross will tell whether the two conditions are identical or not. Inherited diseases in animals are thus pure diseases in a similar sense in which we speak of pure chemicals.

(2) *Abundance of material.*—The study of many human conditions is hampered by their rarity. Inherited diseases in animals can always be obtained in any required quantity at the experimenter's will.

(3) *Controlled environment.*—While human patients generally come from very varied environments and hence often are not strictly comparable, animal material can be kept under very uniform conditions. On the other hand, the influence of environment on the course of a disease can be studied with equal ease by controlled experimentation.

(4) *The study of initial stages.*—For ætiological studies the initial stages of a disease are of the greatest importance, as there are not yet any secondary complications; unfortunately they are often missed in human diseases because patients do not consult the doctor until they have a complaint, and the pathologist in most cases has to reconstruct the course of events in retrospect. These reconstructions cannot compare in precision with the complete series of histological observations which can be obtained with animal material. In human conditions which trace far back in embryonic life we are almost entirely dependent on conjecture, and in the case of many "syndromes" no explanation has even been attempted, whereas in animals complete series of all embryonic stages can be obtained and the relations of events be studied by direct observation.

(5) *Diseases of old age.*—One cannot predict from what cause a healthy young man or woman will die. Hence the inherited basis for diseases of the senium is still largely unknown and unsuspected. In a highly inbred and genetically homogeneous strain of animals (a "pure line" in genetical terminology) this is different; it is common knowledge that pure lines of mice may differ greatly in the incidence of various malignant tumours, including leukæmias; we can thus predict that a certain young mouse will probably develop a specific tumour if it reaches the age of, say, 16 months, while another young mouse from a different strain is very unlikely to do so; the rapid advances in our knowledge about the ætiology of malignant tumours which have been made with the aid of this type of material are so well known that we need not deal with this matter in any great detail. The knowledge of what is going to happen to certain strains of mice makes it possible to study their anatomy and physiology before any tumours appear. If

deal) are at present of any medical interest. But many of these species, harmless at the moment in the presence of their two established and powerful competitors (*rattus* and *norvegicus*), are quite ready to enter, and indeed, wherever there is a chance (as in Central Africa), do enter into association with man and so avail themselves of the security and food which that association confers upon a wild species. So we see that, at any moment, any at present harmless species of this group, given opportunity, may be transformed swiftly into a noxious species of medical or economic importance.

So far we have dealt with merely a few rodents and their parasites in relation to disease. Although forming only an infinitesimal part of the Animal Kingdom and a small part of those animals already known to be of medical importance, they do enable us to form some idea of the complexity of the ecological problems which medical or economic considerations force forwards for solution. In all countries, terrestrial animals and plants are, so to speak, interwoven in a cross-checking system; and in no country can any part of the biota be touched or destroyed without a proportionate and sometimes to our eyes, very disproportionate disturbance of the remainder. The destruction of predatory animals in the interests of stock-raising or for sport; the clearance and cultivation of the land; the production and storage of rich crops of foodstuffs of all kinds; the increase of human populations to great heights or their disappearance as the result of war or pestilence; the construction or destruction of buildings and cities; and the herding together of men and domestic animals; all play their parts in disturbing the balance in favour of some species or to the prejudice of others. Repercussions from such disturbances are bound to follow; sometimes they are detrimental to human interests, more often they are not. In the present state of our knowledge no instructed man can point a finger at any species—not even *Bacillus pestis*—and say with confidence "that species should be exterminated". It is the task of biological science (which, of course, includes medicine) to find out what is the true place in nature and the true function of each living thing; and a further task to devise means of putting troublesome organisms back in their places, of controlling them, and of preventing or curing the ills to which they give rise. After all man himself has created most of the disturbance and it is but just that he should have the painful task of restoring order in a troubled world. He should learn much in the process.

Sound knowledge of ecology can only be based upon sound systematic determinations of the species in every life-chain investigated. Such determinations cannot be made too soon; but they need not be preliminary to an investigation. If good material representing the links of the chain be collected and properly preserved; and if the ecologist or medical worker can recognize those links as distinct things during the progress of his work; the systematic determinations can be made later by the systematists who infest the British Museum, Kew, and other places of the kind. I mention this because no opportunity for observation should ever be lost. But the worker ought to aim at getting sufficient systematic knowledge to enable him to determine at least the commoner forms in any life-chain claiming his attention for himself. It has been difficult in the past to acquire that knowledge. But to-day the systematists are alive to the fact that the world, owing to improved communications of all kinds, is contracting rapidly and that special biological problems, demanding maybe rapid decisions, are likely to come in great numbers as the world is opened up. A great effort is being made therefore to put systematic information in the hands of non-systematic workers in a form which will enable them to apply that knowledge rapidly for themselves as the need arises. In this connexion I may mention Dr. Smart's "Handbook for the Identification of Insects of Medical Importance" and H. E. Hinton and A. Steven Corbet's "Common Insect Pests of Stored Food Products" (Economic Series No. 15), two works published in 1943 by the British Museum (N.H.), as well as two important papers (1) on the larvæ of Lepidoptera (H. E. Hinton) and (2) Keys for the Identification of the Lepidoptera Infesting Stored Food Products (A. S. Corbet and W. H. Tams) which have been collected and published together by the Ministry of Food, 1943.

More biological knowledge, particularly more information concerning the relations of animals to plants and to man is one of the world's chief needs. Elton, with his Bureau at Oxford, has shown us perhaps how to start. But to get all that is needed for medical and economic purposes *a much greater* field than that hitherto ploughed by Elton is indicated and will call for international co-operation. The needs of biology, including medicine, can only be met with the support of an enlightened public.

Finally, I would say that in devising control measures regard should always be paid to ecological knowledge; and bearing in mind the fact that there are no trifles in biology we should watch the effects of our activities unremittingly. We must always be prepared for the unexpected and proceed with caution, not attempting to do more than is necessary to control a species; we cannot get a full knowledge of all the factors in such complex

problems and slight changes in environment, or opportunity may be met by quick and surprising responses not only by organisms immediately under notice, but by many not previously in the picture. I am sure that crude attempts to exterminate certain species, as by laying strychnine baits throughout vast stretches of country, by scattering thallium-treated grain, or by showering down arsenious oxides from the sky, are not sound procedures at all; they may be justified in certain emergencies for a time; but if they became part of an established practice I am sure we should get and deserve sharp punishment in due course from Nature for our presumption.

Animal Genetics

Captain Hans Grüneberg, Royal Army Medical Corps: I prefer to speak about the "Uses and Limitations" rather than about the "Limitations and Uses" of the study of inherited diseases in animals for medical science, and I propose to start this survey by a general consideration of the circumstances which make the study of inherited diseases in animals such a powerful tool for ætiological research.

(1) *"Pure" diseases.*—The current classification of human diseases has in the main been evolved by a process of dichotomy and an example will make this clear. The presence or absence of glucose in the urine divides, in a very rough fashion, the diabetics from the non-diabetics; by a refinement of method (blood sugar curve) we can unmask certain diabetics who fail to excrete glucose; similarly, we can segregate certain types of glycosuria by the fact that they do not react to insulin. In general, the present state of the classification of human diseases is a reflection of the clinical and laboratory methods at our disposal; we can thus never be certain whether a given disease is homogeneous ætiologically, or whether a new technique, diagnostic or therapeutic, will prove it to be a mixture of two similar, but ætiologically different, conditions. Sooner or later we shall reach the last fork of the dichotomy, but there is no way of telling whether this has already happened in any particular instance, and it is safe to say that it has not happened everywhere. Clinical material is thus liable to be heterogeneous, and many inconsistencies are no doubt due to this fact. Inherited diseases in animals, on the other hand, are not defined in successive stages by a process of dichotomy. They come into being as gene mutations, suddenly, clearly delineated, like Athene from the head of Zeus. Their genetical (= ætiological) homogeneity can easily be established by a genetical analysis; and if similar material is obtained from different sources, a cross will tell whether the two conditions are identical or not. Inherited diseases in animals are thus pure diseases in a similar sense in which we speak of pure chemicals.

(2) *Abundance of material.*—The study of many human conditions is hampered by their rarity. Inherited diseases in animals can always be obtained in any required quantity at the experimenter's will.

(3) *Controlled environment.*—While human patients generally come from very varied environments and hence often are not strictly comparable, animal material can be kept under very uniform conditions. On the other hand, the influence of environment on the course of a disease can be studied with equal ease by controlled experimentation.

(4) *The study of initial stages.*—For ætiological studies the initial stages of a disease are of the greatest importance, as there are not yet any secondary complications; unfortunately they are often missed in human diseases because patients do not consult the doctor until they have a complaint, and the pathologist in most cases has to reconstruct the course of events in retrospect. These reconstructions cannot compare in precision with the complete series of histological observations which can be obtained with animal material. In human conditions which trace far back in embryonic life we are almost entirely dependent on conjecture, and in the case of many "syndromes" no explanation has even been attempted, whereas in animals complete series of all embryonic stages can be obtained and the relations of events be studied by direct observation.

(5) *Diseases of old age.*—One cannot predict from what cause a healthy young man or woman will die. Hence the inherited basis for diseases of the senium is still largely unknown and unsuspected. In a highly inbred and genetically homogeneous strain of animals (a "pure line" in genetical terminology) this is different; it is common knowledge that pure lines of mice may differ greatly in the incidence of various malignant tumours, including leukæmias; we can thus predict that a certain young mouse will probably develop a specific tumour if it reaches the age of, say, 16 months, while another young mouse from a different strain is very unlikely to do so; the rapid advances in our knowledge about the ætiology of malignant tumours which have been made with the aid of this type of material are so well known that we need not deal with this matter in any great detail. The knowledge of what is going to happen to certain strains of mice makes it possible to study their anatomy and physiology before any tumours appear. If

we study mouse strains forming a graded series with a tumour incidence ranging from near zero to near 100% and find that these mouse strains for m a similarly graded series as regards some anatomical or physiological peculiarity, it is probable that this second series of differences is somehow connected with the ætiology of the tumour under investigation. Several suggestive relations have recently come to light, and this type of information could not have been obtained from human material. It is perhaps less generally known that the numerous pure lines which are now available provide a most favourable material for the study of the inherited basis of other changes of the senium, both physiological and pathological. This type of study is not possible in man; I cannot say whether I shall develop amyloid degeneration of the kidneys when I grow old; but I can make such a prediction for certain young mice; and if I am interested in whether this senile disease can be mitigated or even prevented I can make experiments with my mice before they have developed the disease.

(6) *Direct methods.*—The diagnostic methods used in human medicine are often indirect, whereas direct methods may be used in experimental animals. Sections of the kidney in every stage of the disease can be examined instead of having to infer its state from the urine produced. In animals, as in man, we can use the success or otherwise of a therapeutic method as a tool in ætiological research; in animals, but not in man, we can also use the converse method and subject the "patient" to experiments designed to make the condition worse.

The advantages of method outlined above are great. The most important group of animals for our studies are the laboratory rodents. If these animals are approached with a knowledge of human anatomy, embryology, histology and physiology, the resemblances with man heavily preponderate over the differences and the diseases of rabbit, guinea-pig, rat and mouse may be expected to show far-reaching similarities with human diseases. Experience shows that this is indeed the case, and in some instances one can go as far as to say that corresponding conditions are not only analogous, but in fact identical. This great similarity of many conditions must, of course, not delude us into an uncritical attitude, and in every case a thorough examination is required to show to what extent comparisons will be valid.

But even if we find that an inherited disease of the rat has no known counterpart in man, its analysis will still be of interest from the medical point of view. For every inherited disturbance of the development or functioning of the body is an experiment performed by Nature herself, and any insight into the physiology of these processes will ultimately, though sometimes very indirectly, be of benefit for the understanding of the working of the human body in health and disease.

To give a balanced survey of the raw material that is awaiting study is a task which is impossible within the confines of a short article.[1] An attempt will be made to give a rough survey of the inherited diseases known in the laboratory rodents, most of which are determined by simple recessive genes.

(A) *Central nervous system.*—Amongst the gross malformations, *pseudencephaly* in the mouse is a well-investigated example. *Otocephaly* in the guinea-pig has a complex genetical basis. Cyclopia in the rabbit, like rhachischisis in the same animal, is still awaiting a detailed study. Milder forms of spina bifida accompany several mutants in the mouse which have more conspicuous effects on the vertebral column, notably on the tail. Amongst the less serious malformations, *syringomyelia* in the rabbit is particularly noteworthy, as it resembles the human disease very closely both clinically and pathologically; the manifestation of the gene is apparently considerably influenced by factors of the environment which now form the subject of detailed investigations. *Absence of the corpus callosum* in the mouse has no demonstrable clinical effects and cannot be diagnosed in the living animal. A very severe (lethal) form of *congenital hydrocephalus* in the mouse is due to a transitory disturbance of the early cartilage and associated with various other effects. Congenital hydrocephalus associated with brachygnathia and dwarfism, and not quite so lethal as the gene in the mouse, has been described in the rabbit; in this case an involvement of some endocrine gland has been suggested, but the evidence for this is not very strong. *Hydrocephalus* of later onset is common in the mouse; three different types have been described; in one of these there is an obstruction of the aqueduct of Sylvius; in another form, which is associated with a discharge of liquid from the nose, the mechanism is probably quite different. An early embryonic disturbance of the distribution of the cerebrospinal fluid is probably responsible for a complex syndrome in the mouse, "*myelencephalic blebs*", which ultimately leads to very variable malformations of the eyes and feet, and which sometimes involves absence of the kidneys, hemilateral or bilateral. *Spastic spinal paralysis* in the rabbit is due to an abnormality of the pyramidal

---

[1] A book on the subject with the necessary documentation is now in the process of preparation.

tracts, while both "shaking paralysis" and "ataxia" in the same animal are two different inherited diseases which seem to involve the extrapyramidal system; a somewhat similar "tremor" occurs as an inherited disease in the American deer-mouse *Peromyscus*. *Epilepsy* in the rabbit is an accompaniment of a certain coat colour mutation and very similar to genuine epilepsy in man; various types of epileptiform seizures also occur in *Peromyscus*; some of these are provoked exclusively by auditory, others exclusively by olfactory stimuli. Genetic differences of susceptibility to "audiogenic" epileptoid seizures seem also to occur in the rat.

(B) *The organ of hearing.*—Most of these diseases, in addition to a labyrinthine involvement, are probably also disturbances of the brain, particularly of the basal ganglia, but the histopathological evidence is still very incomplete. In the mouse, there are no less than eight different kinds of inherited deafness, each due to a different recessive gene. In five of these (*waltzer, shaker*—1, shaker—2, jerker and "Kreissler") there is a characteristic triad of symptoms including spontaneous circular movements, choreic head movements in dorso-ventral direction and deafness from about the fourth week of life onwards. In the three other mutants, the same triad is associated with other anomalies: in one case it regularly occurs together with syndactylism; in "fidget" it is associated with a corneal disease and sometimes with polydactylism of the hind feet; the head shaking in this case is from side to side rather than in dorso-ventral direction, and deafness develops late in life after a period of hyperacuity. The most extreme form is *shaker-short* which also involves an encephalocele, abortive differentiation of the ear vesicles, a shortening of the tail and complete sterility in both sexes. In the mouse there are also some mutants which circle without being deaf, and a similar gene is known in the rat. A comparable range of diseases occurs in *Peromyscus*, and some of these conditions are associated with the epileptiform states mentioned above.

(C) *The eye.*—*Anophthalmia* in the mouse is due to an arrest of development of the optic vesicle. Less severe is *coloboma retinæ* with microphthalmia and orbital cysts in the rabbit, and similar conditions have also been found in the rat and in the guinea-pig. A very interesting type of coloboma retinæ has recently been described in the mouse; in this case the anomaly is regularly associated with a new type of albinism (distinct from ordinary albinism), with a retention of the incisor teeth and with abnormalities of the whiskers (vibrissæ). *Absence of the rods from the retina* in the mouse is due to an arrest of development, while *degeneration of the retina with cataract* in the rat, while in some stages rather similar to rodless, closely resembles certain types of retinitis pigmentosa in man. Two different types of uncomplicated *cataract* have been found in the rat and one in the rabbit; in the rat there is also a kind of cataract associated with dwarfism. A very variable anomaly of the anterior segment of the eye occurs in the mouse: the effects of this gene may include aphakia, persisting pupillary membrane, corneal opacities, microphthalmia and others. *Congenital hydrophthalmus* (buphthalmus) occurs in the rabbit, and a secondary keratitis due to trichiasis is commonly found in "Rex" rabbits. This list is far from complete, and systematic studies will undoubtedly soon increase the range of available material considerably.

(D) *Endocrine organs.*—The classical case is *pituitary dwarfism* in the mouse with absence of the eosinophil cells from the hypophysis; all the endocrine ramifications can be cured by substitution therapy. Inherited *dwarfism* in the rabbit may also have an endocrine basis, but so far therapeutic attempts have not been very effective. The same applies to another kind of dwarfism in the rabbit associated with brachygnathia and hydrocephalus (*see above*), and to dwarfism with cataract in the rat. Dwarfism in the guinea-pig is probably chrondrodystrophic in nature. An inherited state of *latent diabetes* in the rat is probably due to an increased function of the pituitary. *Sexual hypogenesis* in the guinea-pig has been ascribed to a deficiency of the gonad-stimulating hormone of the pituitary, while *duplication of the seminal vesicles* in the mouse is probably due to a hypersecretion of testicular hormone (androgen). Congenital palsy in the guinea-pig is probably a tetany due to hypogenesis of the parathyroids. Endocrine disorders of one kind or another are undoubtedly present in the yellow mouse, which shows early sterility, obesity and a reduced basal metabolism; and there are various structural anomalies and variations within physiological limits in the mouse which have not yet been subjected to a physiological study. Genes thus frequently affect the body through the endocrine system, and we can expect to obtain invaluable information about that system from the very selective effects which genes exercise upon it.

(E) *The blood.*—Both in the mouse and in the rat there occur several inherited anæmias which are of considerable medical interest, though most of them seem to have no known counterparts in man. A *macrocytic anæmia* in the mouse occurs in two modifications, one of which is so severe that it proves fatal within a few days after birth, while the other is much milder; by combination of these two types and with normal mice, a series can be

built up from an exceedingly mild anæmia, which makes no clinical symptoms whatsoever and can only be discovered by extensive laboratory investigations, up to the completely fatal type. The anæmia does not react to liver preparations, but even the most-extreme type can be kept alive indefinitely by intraperitoneal blood injections. A rapidly fatal anæmia in the rat develops after birth and is characterized by spherocytosis and jaundice. Another anæmia in the rat is still more similar to acholuric jaundice in man; newly born young are heavily jaundiced, the cells are microcytes and show increased fragility, and the spleen is enlarged; splenectomy does, however, not cure the condition; affected animals survive to maturity. An anæmia associated with splenomegaly has recently been described in the mouse. Though the *siderocyte anæmia* of the mouse has no known parallel in man, its investigation has already produced some facts of clinical importance; the anæmia is embryonic and transitory and characterized by the presence of hypochromic cells with free iron (siderocytes); it has since been shown that such cells are a normal feature in the embryonic life of several mammals, including man, and that they can reappear in the blood of adult humans under pathological conditions; it has recently been suggested that siderocytes are old red cells just as reticulocytes are young erythrocytes; their systematic study in man is likely to prove of practical importance. We mention in passing the occurrence, in pigs, of a condition comparable to hæmophilia in man, though it is not confined to the male sex. Finally, there are the inherited leukæmias in the mouse, which may properly be classified as tumours of the blood.

(F) *Skeleton.*—A very characteristic *hypertrophy of the cartilage* in the rat leads to numerous complications, notably in the thorax, with arrest of lung development (superficially resembling an emphysema) and disturbances of the circulation which ultimately prove fatal. We have already mentioned the transitory cartilage anomaly of the mouse resulting in congenital hydrocephalus, and the achondroplasia of the guinea-pig. In the *greylethal* of the mouse, there is a complete absence of secondary bone absorption with retention of the whole dentition; associated effects are absence of yellow pigment from the fur and a disturbance of the phosphorus metabolism. The genetically very complex series of *short-tail* and *taillessness* in the mouse is ultimately due to early embryonic anomalies of the notochord. Other tail anomalies, like Kinky-tail and pig-tail, await more detailed studies. *Flexed-tail* (another manifestation of siderocyte anæmia mentioned above) is due to faulty histological differentiation of the intervertebral discs. *Absence of the tibia* in the mouse closely resembles certain deficiencies of long bones in man. *Polydactylism* in the guinea-pig tends to restore the pentadactyl foot in heterozygous condition, but produces complex monstrosities in the homozygotes; other uncomplicated types of polydactylism are known in the mouse (*see also above*), in which there is also inherited oligodactylism; various types of foot anomalies also occur in myelencephalic blebs (*see above*). *Brachydactylism* in the rabbit has been traced back to peripheral disturbances in the embryonic circulation. *Skull shape anomalies* due to premature synostosis of sutures are known in the rabbit, while several trivial skull variants (supernumerary bones, etc.) have been described in the mouse. We mention here an extreme monstrosity in the mouse which in several cases leads to a duplication of the posterior half of the body with profound changes in the urogenital system and the distal part of the alimentary tract.

(G) *Digestive tract.*—The number of diseases so far described is small. *Harelip and cleft palate* in the mouse is an almost photographic counterpart of the human condition and genetically complex; there are some indications that its incidence can be influenced by hormone treatment of the pregnant female. Certain gross monstrosities of the whole head region have been described in the mouse, and a stenosis of the œsophagus, probably genetic in origin, has recently been discovered in the same animal. Certain hyperplastic changes in the mucosa of the stomach are characteristic for one pure line of mice. Atresia ani is regularly found in Danforth's short tail (*see below*). Umbilical hernia in the rat may be mentioned here.

(H) *Urogenital system.*—We have already mentioned the absence of kidneys which occurs in certain substrains of myelencephalic blebs in the mouse, often accompanied by hydronephrosis. The gene for *Danforth's short-tail* in the mouse, in addition to its skeletal effects, reduces the kidneys to varying degrees in the heterozygotes and causes their complete absence, together with atresia ani and other deformities, in the homozygotes. Inherited kidney anomalies have also been described in the rat. A condition similar to *amyloid degeneration of the kidney* in man is peculiar to the senium of one pure line of mice, while another tends to develop *cystic kidneys* in old age. *Imperforate vagina* in the mouse has no endocrine basis in contradistinction to the genital abnormalities described under (D). There are also structural differences of the mammary glands which have come to light in connexion with work on breast cancer in the mouse.

(I) *Tumours.*—The complex situation of mammary tumour formation, partly under chromosomal control and partly conditioned by a factor transmitted through the milk, has

built up from an exceedingly mild anæmia, which makes no clinical symptoms whatsoever and can only be discovered by extensive laboratory investigations, up to the completely fatal type. The anæmia does not react to liver preparations, but even the most extreme type can be kept alive indefinitely by intraperitoneal blood injections. A rapidly fatal anæmia in the rat develops after birth and is characterized by spherocytosis and jaundice. Another anæmia in the rat is still more similar to acholuric jaundice in man; newly born young are heavily jaundiced, the cells are microcytes and show increased fragility, and the spleen is enlarged; splenectomy does, however, not cure the condition; affected animals survive to maturity. An anæmia associated with splenomegaly has recently been described in the mouse. Though the *siderocyte anæmia* of the mouse has no known parallel in man, its investigation has already produced some facts of clinical importance; the anæmia is embryonic and transitory and characterized by the presence of hypochromic cells with free iron (siderocytes); it has since been shown that such cells are a normal feature in the embryonic life of several mammals, including man, and that they can reappear in the blood of adult humans under pathological conditions; it has recently been suggested that siderocytes are old red cells just as reticulocytes are young erythrocytes; their systematic study in man is likely to prove of practical importance. We mention in passing the occurrence, in pigs, of a condition comparable to hæmophilia in man, though it is not confined to the male sex. Finally, there are the inherited leukæmias in the mouse, which may properly be classified as tumours of the blood.

(F) *Skeleton.*—A very characteristic *hypertrophy of the cartilage* in the rat leads to numerous complications, notably in the thorax, with arrest of lung development (superficially resembling an emphysema) and disturbances of the circulation which ultimately prove fatal. We have already mentioned the transitory cartilage anomaly of the mouse resulting in congenital hydrocephalus, and the achondroplasia of the guinea-pig. In the *greylethal* of the mouse, there is a complete absence of secondary bone absorption with retention of the whole dentition; associated effects are absence of yellow pigment from the fur and a disturbance of the phosphorus metabolism. The genetically very complex series of *short-tail* and *taillessness* in the mouse is ultimately due to early embryonic anomalies of the notochord. Other tail anomalies, like Kinky-tail and pig-tail, await more detailed studies. *Flexed-tail* (another manifestation of siderocyte anæmia mentioned above) is due to faulty histological differentiation of the intervertebral discs. *Absence of the tibia* in the mouse closely resembles certain deficiencies of long bones in man. *Polydactylism* in the guinea-pig tends to restore the pentadactyl foot in heterozygous condition, but produces complex monstrosities in the homozygotes; other uncomplicated types of polydactylism are known in the mouse (*see also above*), in which there is also inherited oligodactylism; various types of foot anomalies also occur in myelencephalic blebs (*see above*). *Brachydactylism* in the rabbit has been traced back to peripheral disturbances in the embryonic circulation. *Skull shape anomalies* due to premature synostosis of sutures are known in the rabbit, while several trivial skull variants (supernumerary bones, etc.) have been described in the mouse. We mention here an extreme monstrosity in the mouse which in several cases leads to a duplication of the posterior half of the body with profound changes in the urogenital system and the distal part of the alimentary tract.

(G) *Digestive tract.*—The number of diseases so far described is small. *Harelip and cleft palate* in the mouse is an almost photographic counterpart of the human condition and genetically complex; there are some indications that its incidence can be influenced by hormone treatment of the pregnant female. Certain gross monstrosities of the whole head region have been described in the mouse, and a stenosis of the œsophagus, probably genetic in origin, has recently been discovered in the same animal. Certain hyperplastic changes in the mucosa of the stomach are characteristic for one pure line of mice. Atresia ani is regularly found in Danforth's short tail (*see below*). Umbilical hernia in the rat may be mentioned here.

(H) *Urogenital system.*—We have already mentioned the absence of kidneys which occurs in certain substrains of myelencephalic blebs in the mouse, often accompanied by hydronephrosis. The gene for *Danforth's short-tail* in the mouse, in addition to its skeletal effects, reduces the kidneys to varying degrees in the heterozygotes and causes their complete absence, together with atresia ani and other deformities, in the homozygotes. Inherited kidney anomalies have also been described in the rat. A condition similar to *amyloid degeneration of the kidney* in man is peculiar to the senium of one pure line of mice, while another tends to develop *cystic kidneys* in old age. *Imperforate vagina* in the mouse has no endocrine basis in contradistinction to the genital abnormalities described under (D). There are also structural differences of the mammary glands which have come to light in connexion with work on breast cancer in the mouse.

(I) *Tumours.*—The complex situation of mammary tumour formation, partly under chromosomal control and partly conditioned by a factor transmitted through the milk, has

Section of Proctology

President—CUTHBERT E. DUKES, O.B.E., M.D.

[*November* 10, 1943]

The Surgical Pathology of Rectal Cancer

PRESIDENT'S ADDRESS

By CUTHBERT E. DUKES. O.B.E.. M.D.. M.Sc., D.P.H.

As pathologist to St. Mark's Hospital I have three advantages over others who have studied the principles of the pathology of rectal cancer. In the first place since my laboratory has been in receipt of operation specimens from a number of different surgeons it has been possible for me to collect a larger series of cases than any one surgeon could collect from his own practice within existing limits of human capacity and span of life. Secondly, the collection of material from different surgical sources results in the pooling of experience and so gives a more comprehensive picture than the published results of any one individual. Thirdly, I have had free access to the follow-up records at St. Mark's Hospital. This has enabled me to watch the progress of more than 1,000 patients treated by excision of the rectum, in each of whom my laboratory report has recorded the size and position of the primary tumour and the extent of local, venous and lymphatic spread. The slow unfolding of the after-history of this big series has been an impressive experience, as one by one the real significance of each fact has been made clear.

The general object of this paper is to define as precisely as possible the significance of each fact observed during the naked-eye and microscopic examination of an operation specimen of cancer of the rectum. There are two ways of assessing the significance of the phenomena we are dealing with : (1) By recording how often they occur, and (2) by watching their influence on survival after operation. Take for instance the discovery of a clump of cancer cells in a branch of the hæmorrhoidal vein. To interpret the significance of this we need to know in what proportion of cases of rectal cancer this is found and also how it affects survival rate. Each fact which can be established with regard to local, venous and lymphatic spread has a certain value, something which is worth taking into consideration when planning operations or in formulating prognosis.

Pathological technique.—I am now going to invite you to follow to the laboratory the organ the surgeon has removed in the operating theatre. Valuable information may be missed unless the operation specimen is pinned out and sewn to a frame before being fixed in formalin. This pinning out need not be done at once. If the specimen is to be despatched elsewhere the best plan is to take the whole organ as removed from the body and enclose it first in a piece of damp gauze, then a layer of dry cotton-wool and finally wrap it up in jaconet or a large towel (not forgetting to attach to the outside of the parcel the name, age and sex of the patient). An operation specimen so treated can be kept for a day or two without deterioration, though naturally it is better for it to be pinned out and fixed with as little delay as possible. It is well known that solid organs and small bits of tissue like biopsy fragments are best placed directly into a fixative solution like 10% formalin, but few surgeons realize that this procedure is ruinous for a hollow viscus or a segment of intestine; these should always either be packed with cotton-wool or pinned out on a frame before fixation. Fixation of an operation specimen takes about twenty-four hours but no harm will come from leaving the pinned-out specimen in the formalin for two or three days. It may then be removed from its frame and washed with water.

LOCAL SPREAD

The significance of the position, size and shape of the primary growth is the first point to be considered. The position of a cancer may be of significance because the three regions into which the rectum is usually divided namely, the lower "third", the ampulla and the upper "third", differ in their blood supply and field of lymphatic drainage. In passing, it may be observed that nowadays we label as cancers of the rectum all columnar-cell malignant tumours which are removed by the operation of rectal excision. This results in the including as "tumours of the rectum" some growths which

FEB.—PROCT. 1

Section of Proctology

President—Cuthbert E. Dukes, O.B.E., M.D.

[*November* 10, 1943]

The Surgical Pathology of Rectal Cancer

PRESIDENT'S ADDRESS

By Cuthbert E. Dukes, O.B.E., M.D., M.Sc., D.P.H.

As pathologist to St. Mark's Hospital I have three advantages over others who have studied the principles of the pathology of rectal cancer. In the first place since my laboratory has been in receipt of operation specimens from a number of different surgeons it has been possible for me to collect a larger series of cases than any one surgeon could collect from his own practice within existing limits of human capacity and span of life. Secondly, the collection of material from different surgical sources results in the pooling of experience and so gives a more comprehensive picture than the published results of any one individual. Thirdly, I have had free access to the follow-up records at St. Mark's Hospital. This has enabled me to watch the progress of more than 1,000 patients treated by excision of the rectum, in each of whom my laboratory report has recorded the size and position of the primary tumour and the extent of local, venous and lymphatic spread. The slow unfolding of the after-history of this big series has been an impressive experience, as one by one the real significance of each fact has been made clear.

The general object of this paper is to define as precisely as possible the significance of each fact observed during the naked-eye and microscopic examination of an operation specimen of cancer of the rectum. There are two ways of assessing the significance of the phenomena we are dealing with: (1) By recording how often they occur, and (2) by watching their influence on survival after operation. Take for instance the discovery of a clump of cancer cells in a branch of the hæmorrhoidal vein. To interpret the significance of this we need to know in what proportion of cases of rectal cancer this is found and also how it affects survival rate. Each fact which can be established with regard to local, venous and lymphatic spread has a certain value, something which is worth taking into consideration when planning operations or in formulating prognosis.

Pathological technique.—I am now going to invite you to follow to the laboratory the organ the surgeon has removed in the operating theatre. Valuable information may be missed unless the operation specimen is pinned out and sewn to a frame before being fixed in formalin. This pinning out need not be done at once. If the specimen is to be despatched elsewhere the best plan is to take the whole organ as removed from the body and enclose it first in a piece of damp gauze, then a layer of dry cotton-wool and finally wrap it up in jaconet or a large towel (not forgetting to attach to the outside of the parcel the name, age and sex of the patient). An operation specimen so treated can be kept for a day or two without deterioration, though naturally it is better for it to be pinned out and fixed with as little delay as possible. It is well known that solid organs and small bits of tissue like biopsy fragments are best placed directly into a fixative solution like 10% formalin, but few surgeons realize that this procedure is ruinous for a hollow viscus or a segment of intestine; these should always either be packed with cotton-wool or pinned out on a frame before fixation. Fixation of an operation specimen takes about twenty-four hours but no harm will come from leaving the pinned-out specimen in the formalin for two or three days. It may then be removed from its frame and washed with water.

LOCAL SPREAD

The significance of the position, size and shape of the primary growth is the first point to be considered. The position of a cancer may be of significance because the three regions into which the rectum is usually divided namely, the lower "third", the ampulla and the upper "third", differ in their blood supply and field of lymphatic drainage. In passing, it may be observed that nowadays we label as cancers of the rectum all columnar-cell malignant tumours which are removed by the operation of rectal excision. This results in the including as "tumours of the rectum" some growths which

are actually situated in the distal end of the pelvic colon. The operating surgeon has insidiously enlarged the boundaries of the rectum at the expense of the colon, a fact which should not be forgotten if comparisons are made with statistics of a former period.

Are the results of surgical treatment the same whether the cancer is situated in the lower third, the ampulla or the upper third? I have followed up 370 cases treated by a combined operation (abdomino-perineal or perineo-abdominal) during the years 1930 to 1939. The cases were divided into sub-groups according to the extent of local and lymphatic spread and comparisons made for three-year and five-year survivals. This analysis showed that for cases *without* glandular metastases the results of surgical treatment were approximately the same whatever the situation of the primary growth, but for cases *with* glandular metastases the results varied to some extent with the position in the rectum of the malignant growth. For cancers with lymphatic metastases situated in the rectal ampulla the results of surgical treatment were not so good as for growths of a similar stage of development in the upper and lower third. No doubt this is due to the fact that lymphatic spread from ampullary growths is more likely to pass laterally along the course of the middle hæmorrhoidal vessels but this cannot be a frequent occurrence because the difference in the survival rate of patients with growths in different regions of the rectum is slight, and with the present series of cases only of doubtful statistical significance. Judgment should be reserved till a larger series of cases have been observed over a longer period, but most likely in the end the figures will show that the worst place to have a rectal cancer with lymphatic metastases is in the rectal ampulla.

The size and surface area of a rectal cancer is of less importance than might be anticipated. A very early growth is most likely to be small and a very advanced growth may be large but there is no direct relationship between the surface area and the extent of lymphatic or venous spread. A small shallow ulcer of high grade malignancy may have spread far and wide in lymphatic and venous channels, whereas a fungating growth of much larger dimensions may still be localized to the submucosa and rectal muscle. Shape is of more importance than size. Protuberant growths are often of a low grade of malignancy and tend to metastasize late. On the other hand deep ulceration is usually a sign of deep penetration into the perirectal tissues and indicates a greater probability of lymphatic metastases. The significance of the difference between protuberant and ulcerating growths was recognized by the surgeon who declared that he was more afraid of a tumour which grew away from him than of one which grew towards him.

There is not much to be said about the extent to which a rectal cancer may spread within the bowel wall above or below its visible naked-eye boundaries except that such intramural infiltration is rare. A rectal cancer seems generally to enlarge equally in all directions superficially from a central focus in the mucous membrane, but as a rule the lateral surface spread in the transverse axis proceeds faster than the upward and downward spread in the long axis, thus accounting for the oval shape. The limits of the growth within the submucosa are often a little wider than in the mucous membrane, but apart from this it is rare to find any extension within the rectum itself, either above or below the margin of the surface growth. This fact is of importance in cancers of the upper third of the rectum treated by perineal excision because in cases without lymphatic metastases this operation has often proved satisfactory even when it was only possible to get just above the growth.

It is the lot of the surgeon often to meet with disappointment because some circumstance over which he has no control frustrates his labours in a case he has expected to do well. It is also true that sometimes a patient survives in defiance of well-founded expectations of an early decease. The recollection of such pleasant surprises helps us "to walk cheerfully through the world".

A male patient (B. S.), aged 54, with very extensive cancer of the rectum, was treated by "palliative" perineal excision in June 1939. The operation was difficult and seemed unsatisfactory not only because of the enormous size of the growth but also on account of dense adhesions. When the operation was completed the house surgeon wrote in the notes "as much as possible of the growth and lower rectum was removed", and my report on the operation specimen stated that there was no free margin above and it looked as if only a portion of the tumour had been removed (fig. 1). So a fortnight later the "redundant" growth was removed by diathermy and radium needles inserted (3 × 10 mg. for five days and 6 × 2 mg. for nine days=6,192 mg. hours). The wound healed and the patient was discharged from hospital. He returned to his work as a retail tradesman and has remained well with no signs of recurrence for more than four years.

VENOUS SPREAD

As soon as a malignant tumour invades the submucosa it reaches a region richly supplied with small veins. Later when the growth has spread to the perirectal fat it comes in close proximity to the hæmorrhoidal veins and their tributaries. The passage of can-
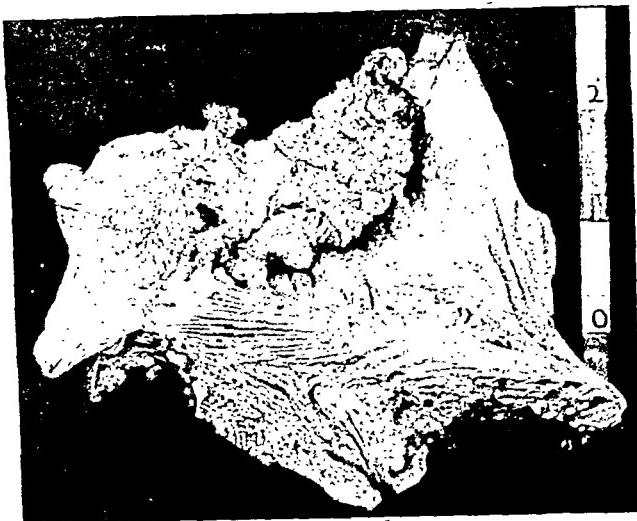
FIG. 1.—Palliative perineal excision for fixed carcinoma in lower third of rectum. Photograph of operation specimen showing only partial removal of growth.

SURFACE VIEW OF MALIGNANT GROWTHS IN RECTUM

ROOTLIKE EXTENSION OF GROWTH INTO VEINS IN PERIRECTAL FAT.

FIG. 2.—Patient (5582) died from hepatic metastases three and a half years after excision of the rectum.

cerous emboli along the hæmorrhoidal veins may give rise to hepatic metastases and so it is natural to ask if any information as to whether or not this disaster has occurred can be obtained by the dissection of the veins in an operation specimen. It is of course obvious that an embolus composed of cancer cells might travel up the hæmorrhoidal vein without leaving any trace behind. This being so, the latent existence of hepatic metastases cannot be excluded because nothing is found in the veins of the operation specimen, but in some cases when the vein is dissected a solid clump of cancer cells can actually be demonstrated in the hæmorrhoidal vein or one of its tributaries. As a rule such an intravenous extension remains in continuity with the primary growth and appears as a root-like process pushed out for a variable distance along the lumen of the vein as though along the path of least resistance (fig. 2).
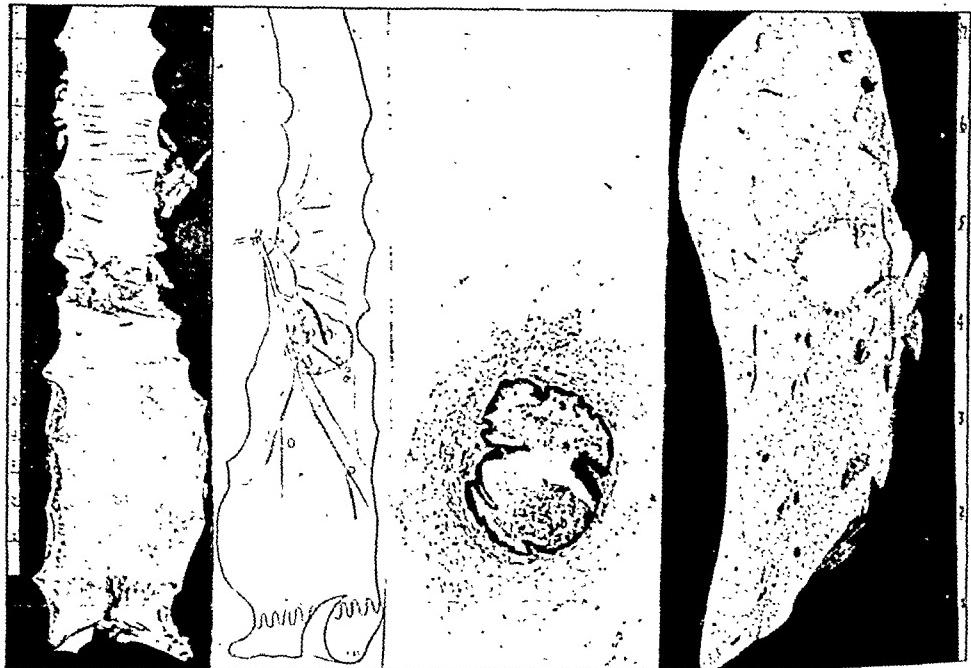
Operation specimen and gland dissection Section of hæmorrhoidal vein Slice through liver at autopsy

FIG. 3.
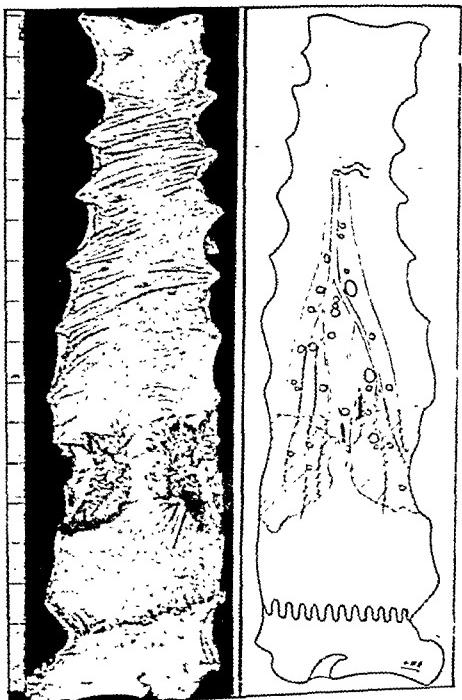
FIG. 4.—Dissected operation specimen showing extension of carcinoma within two tributaries of the superior hæmorrhoidal vein. Patient (No. 838) has survived five years.
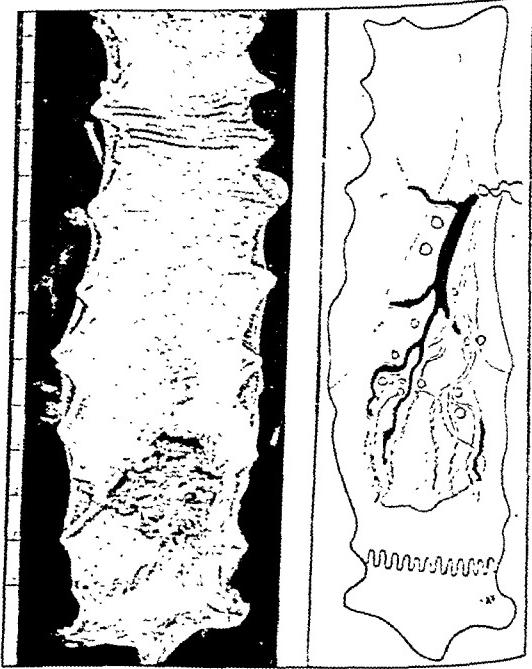
FIG. 5.—Dissected operation specimen of rectal cancer showing massive thrombosis and extension of the malignant growth along the superior hæmorrhoidal vein. Patient H. G. alive and well six years later.

One of the first patients in whom this intravenous extension was noticed died a few days after the operation for cancer of the rectum and the post-mortem examination revealed a small hepatic metastasis (fig. 3). So we decided to make the dissection of the veins part of the routine examination of all operation specimens of rectal cancer to see how often venous spread could be demonstrated and also in fatal cases to correlate post-mortem findings with the results of vein dissections.

More than 1,000 operation specimens of rectal cancer have now been examined for the presence of cancer cells in the hæmorrhoidal vein or its tributaries and the type of intravenous spread just described has been found in 17%, so it is not really a rare phenomenon. It occurs with equal frequency in all regions of the rectum, and though commoner in advanced growths with lymphatic metastases, it may also be found in tumours at an early stage of development. Its closest correlation is with the histology of the primary tumour, an association which is very definite and convincing. The more rapid the growth the greater the likelihood of venous spread. Evidence of venous spread has been found in less than 5% of all well-differentiated slow-growing rectal cancers (Grade I), whereas in anaplastic growths of high-grade malignancy (Grade IV) it is demonstrable in more than 31% of cases (Table I).

TABLE I.—INFLUENCE OF HISTOLOGY OF TUMOUR ON INCIDENCE OF VENOUS SPREAD

Grade of primary tumour	Number of cases	Percentage with venous spread
1	81	4·9
2	442	11·8
3	179	25·4
4	19	31·6
Colloid	107	19·5

In collecting information from post-mortem examinations the first point was to decide whether or not the presence of demonstrable growth in the hæmorrhoidal vein of an operation specimen is or is not always associated with hepatic metastases. Opportunity for a full post-mortem examination has now been obtained in 63 patients who have died within a week or two of excision of the rectum; in all of these a dissection of the hæmorrhoidal veins had been made. In 20 of these 63 cases malignant growth had been noticed in the hæmorrhoidal vein or one of its tributaries and at first it was assumed that hepatic metastases would be found in all these cases. Actually metastases were found in only 10 of these 20 cases. It gradually became clear that no certain forecast of hepatic metastases can be made from the finding of malignant growth in the hæmorrhoidal vein, although it is undoubtedly true that hepatic metastases are more common in cases with demonstrable venous spread. As the figures stand at present hepatic metastases have been found in exactly half of the cases in which the veins showed carcinomatous extensions, whereas hepatic metastases have been found in only one-quarter of the cases in which the veins were free.

In considering how it can happen that the liver may remain free from metastases although malignant growth has been established in the hæmorrhoidal vein it must be kept in mind that venous spread, like lymphatic, varies in degree. In most of the cases without hepatic metastases the growth in the vein was firmly fixed and slight in extent but hepatic metastases were more commonly found when the intravenous growth had spread for an inch or more along the lumen of a larger vein. Comparisons of the survival rate with and without venous spread leave no doubt that the type of intravascular extension we are considering does adversely affect prognosis. For purposes of comparison I took a group of 400 patients, all of whom have been followed up for five years or more, and contrasted the survival rate of the 58 of these who had had intravenous spread with the 342 who had not. The survival rate was definitely worse for the venous spread group but it would be incorrect to attribute this entirely to one cause.

Allowance must be made for the fact that venous spread is commoner in tumours of a high grade of malignancy and is also generally associated with lymphatic metastases, that is to say, venous spread is often associated with other factors which decrease prospects of survival after operation. The fairest comparison would be between cases with and those without venous spread, all being of the same grade and all without lymphatic metastases, but if calculations are based on those alone then numbers are much reduced because venous spread is less common in cases without lymphatic metastases. For this reason it would seem to be premature to publish all the figures at present, especially in view of the fact that only about one-third of all the cases in which vein dissections have been carried out have so far been under observation for a full five years. Therefore this should be regarded only as a preliminary survey of material which at a later date can be subjected to more exact statistical analysis. In the meantime I think the following simple generalizations are likely to stand the test of time. The discovery of a clump of cancer cells in the hæmorrhoidal vein adversely affects
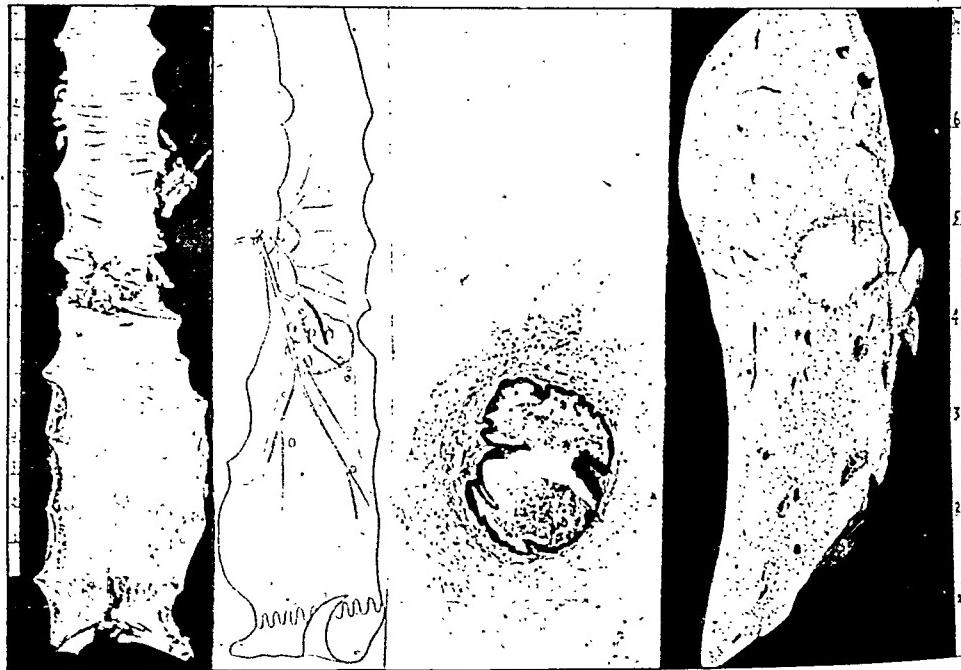
Operation specimen and gland dissection   Section of hæmorrhoidal vein   Slice through liver at autopsy

FIG. 3.
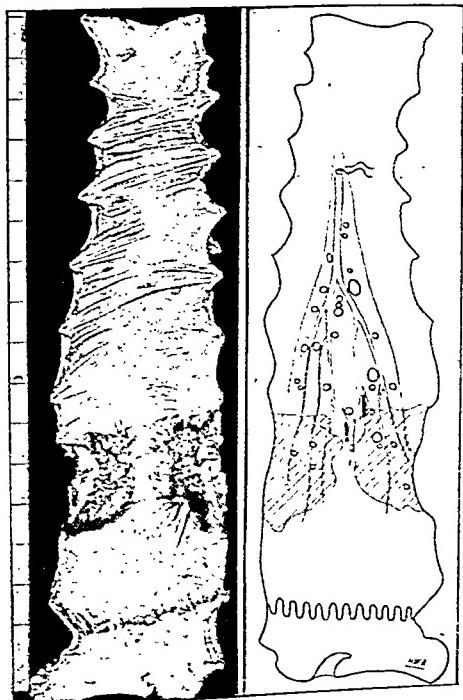
FIG. 4.—Dissected operation specimen showing extension of carcinoma within two tributaries of the superior hæmorrhoidal vein. Patient (No. 838) has survived five years.
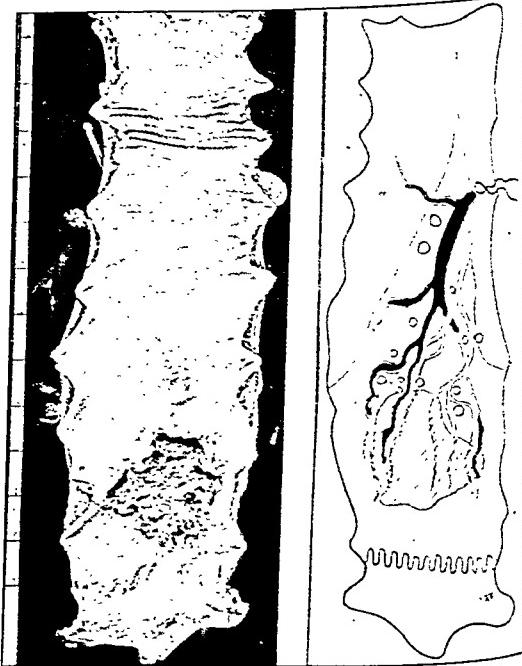
FIG. 5.—Dissected operation specimen of rectal cancer showing massive thrombosis and extension of the malignant growth along the superior hæmorrhoidal vein. Patient H. G. alive and well six years later.

Passing from the number of glands to the much more important question of lymphatic metastases we find here also a surprising variability. Lymphatic metastases may be many or few but from the size and shape of the rectal cancer it is rarely possible to predict how many will be found. There is, however, a close relation between the histological grade of the primary tumour and the presence of lymphatic metastases; an even closer relationship than was shown to exist between histological grade and venous spread. Metastases are comparatively rarely found in well-differentiated growths of a low grade of malignancy (Grade I) but are almost invariably present in rapidly growing anaplastic tumours (Grade IV). The incidence of lymphatic metastases in each histological grade (Broder's method) is shown by an analysis of 1,262 cases recorded in Table IV. These

TABLE IV.—RELATION OF LYMPHATIC METASTASES TO HISTOLOGICAL GRADE OF TUMOUR (1,262 CASES)

Tumour grade	Number of cases	Percentage with lymphatic metastases
1	101	16·8
2	694	42·5
3	286	73·8
4	23	95·5
Colloid	158	72·1

figures provide a very convincing proof of the importance of microscopic examinations and of the value of grading tumours on the basis of their histology. There are of course no sharply defined boundaries to the grades; grading is an artificial division into four arbitrary groups and some difficulty is likely to be expected therefore in labelling tumours which appear to be intermediate in character, but when the necessary experience in grading has been gained there is no doubt that a forecast of the extent of lymphatic metastases can often be given from a study of the histology of a rectal cancer especially for the extreme grades I and IV.

The total number of glandular metastases is also often closely related to the grade of the primary tumour. It may be stated as a general rule that the greater the number of lymphatic metastases the worse the prognosis is likely to be, but in a survey of a large series of cases one is tempted to go further than this and to ask if any special significance can be attached to the actual number of metastases. In order to answer this I have worked through our records at St. Mark's dividing up the cases according to the number of lymphatic metastases and comparing the survival rates of cases with one, two, three, four, &c., glandular deposits. Such an analysis shows at once that the prognosis after excision of the rectum for cancer steadily worsens with the increase in the number of metastases especially where more than three or four glands are affected. The follow-up records show that patients with only one to three lymphatic metastases often survive five years but this fifth anniversary is rarely reached by patients with four or five metastases. Here is a generalization easy to remember. Patients with five or more metastases rarely live for five years.

The position of glandular metastases is of even greater importance than their number. Any form of lymphatic spread adversely affects prognosis but the simple division of cases into those with and those without lymphatic metastases ordinarily used for statistical calculations takes no account of position.

The importance of the presence of lymphatic metastases is shown by the grouping into A, B and C cases which we have adopted at St. Mark's Hospital. Since this system sometimes has my name attached to it I should like to say that it originated as a continuation of a clinical classification used by Mr. Lockhart Mummery. He divided his cases into favourable, less favourable and unfavourable groups on the basis of his clinical judgment and when I suggested that the classification would be more generally useful if based on pathological standards he gave it his whole-hearted support. I defined the cases in which the growth was limited to the rectum as A cases, those with extension to the perirectal fat but no lymphatic metastases as B cases and labelled as C cases all those with lymphatic metastases (fig. 7). The follow-up records soon showed this to be a reliable method of assessing prognosis and it has proved particularly useful for comparing cases treated by different operations.

A further subdivision of the C cases was later adopted in order to study the significance of the position of lymphatic metastases. Cases were described as C 2 if the lymphatic metastases extended up to and included the gland nearest the point of ligature of the vascular pedicle. If, however, the lymphatic spread had not reached this level and the glands in this region were free from metastases the case was labelled C I (fig. 8). The striking difference in the survival rates of these two groups will be illustrated in the last section of this paper which deals with the results of operative treatment.

In what fraction of all cases of rectal cancer are lymphatic metastases so situated that

prognosis due to a greater probability of hepatic metastases. In considering the chances of this, attention should be given to the extent and character of venous spread. If this is limited to the outer margin of the primary tumour and firmly fixed it has about the same significance as an isolated lymphatic metastasis (fig. 4), but if the growth within the vein is massive and accompanied by loose clots the passage of emboli to the liver is almost certain. I say "almost certain" because no one who has had the opportunity of observing the vagaries of human cancer would venture to predict the future without reservation.

A man (H. G.), aged 62, was operated on by perineo-abdominal excision in March 1937 (by Mr. W. B. Gabriel). An ulcerating growth three inches in diameter almost completely encircled the lower third of the rectum. There was much local spread into the perirectal fat and the superior hæmorrhoidal vein stood out prominently and felt like a knotted cord. Dissection showed the vein to be completely thrombosed and filled with carcinoma along its entire course, extending right from the primary tumour to the ligature of the vascular pedicle. There was also evidence of retrograde extension along many of the tributaries of the hæmorrhoidal vein, but strangely enough the lymphatic glands were all free from metastases (figs. 5 and 6). The patient made a good recovery from the operation. That was five years ago and he is still alive and well. His perineal wound has completely healed and there is no sign of recurrence or of liver disease. He does a long day's work in an office. He ascribes his good health in part to the fact that he has had nothing to do with doctors for more than three years.

<center>LYMPHATIC SPREAD</center>

The dissection of operation specimens of rectal cancer and the preparation of scale drawings to show the position, size and number of lymphatic metastases have been perfected by my senior assistant, Mr. H. J. R. Bussey, B.Sc. These gland dissections were undertaken at first simply for the purpose of giving to the surgeon as much information as possible about the patient on whom he had operated, but the accumulation of these records and their reconsideration in the light of the patient's after-history is beginning to bring forth a substantial return for the labour involved.

There is an amazing variability in the number of lymphatic glands found during the dissection of operation specimens of rectal cancer. In some cases only one or two glands are to be found whereas in others it may be easy to dissect out more than fifty. In a consecutive series of 596 operation specimens of rectal cancer the average number of glands was 17·4 but there was a very wide "scatter" (Table II). It is obvious that we cannot speak of any fixed normal number of glands but that new lymphoid tissue in varying amount is produced to meet a need and in response to some stimulus.

In rectal cancer the stimulus to proliferation of lymphoid tissue appears to be septic absorption and this depends chiefly on the surface area of the malignant ulceration. Support for this statement is provided by correlating the total number of lymphatic glands with measurement of the size of the primary tumour in the rectum (Table III). Lymphatic

TABLE II.

Number of cases	Number of glands found
25	0– 5
102	6–10
144	11–15
139	16–20
92	21–25
56	26–30
22	31–35
7	36–40
2	41–45
3	46–50
4	50 +
596	

Mean number of glands 17·4.

TABLE III.—RELATION OF SIZE OF TUMOUR TO NUMBER OF GLANDS.

Size of tumour				Mean number of glands
134 large tumours (more than 3 in. in diameter)				21
333 medium tumours (diameter 2 in. to 3 in.)				17·1
129 small tumours (diameter less than 2 in.)				14·5
	Quadrants affected			
263 tumours spread over 4 quadrants				19
206	,,	,, 3	,,	17·4
85	,,	,, 2	,,	14·4
42	,,	,, 1	quadrant	13·2

glands are most numerous in association with big ulcerating growths which are septic in character. The cancerous tissue itself appears to exert little, if any, stimulus to the production of new lymphatic glands. This is shown by the fact that for growths of a similar surface area the total number of lymphatic glands is approximately the same whether the cancer is at an early stage and confined to the rectal muscle or is more advanced and has spread to the perirectal fat. Invasion of lymphatic glands by cancerous growth does not act as a call to the formation of new lymphatic glands on an appreciable scale. Cancerous metastases do of course increase the size of existing lymphatic glands but in operation specimens of rectal cancer of similar size the total number of glands is on an average much the same whether there be many metastases or few.

lymphatic metastases, but when only one or two of the regional glands are affected the disease may still be well within the scope of perineal excision. In one of the cases illustrated in fig. 9 the metastases are within reach of perineal excision, whereas the other case would certainly have had a better chance with a combined operation. The question now to be considered is in what proportion of all cases with glandular metastases has the lymphatic spread passed beyond the reach of a perineal excision, but not beyond a combined operation.

I have tried to answer this question by making a survey of 425 cases with glandular metastases treated by a combined operation, dividing them into two groups, one suitable for a perineal and the other for a combined excision. As so often happens when one tries to draw arbitrary lines where there is no natural boundary I found myself left with a large number of border-line cases in which it was hard to say whether all the affected glands would or would not have been included in the tissue removed by perineal excision. There is of course no constant upper limit to the scope of perineal excision, this varying from case to case. I therefore decided to confine this investigation simply to finding out what proportion of cases with glandular metastases are easily within the
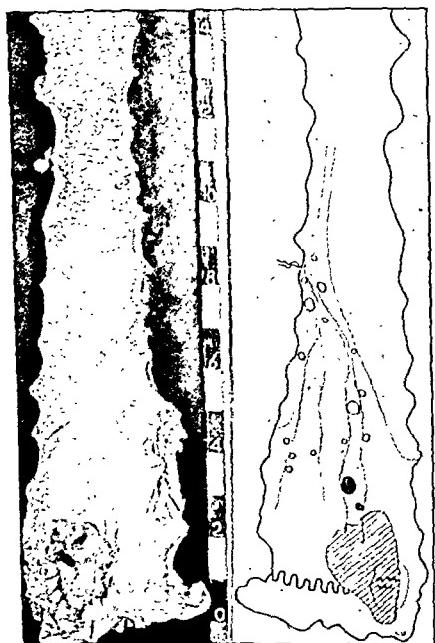
Within scope of perineal excision.　　　　Beyond scope of perineal excision.
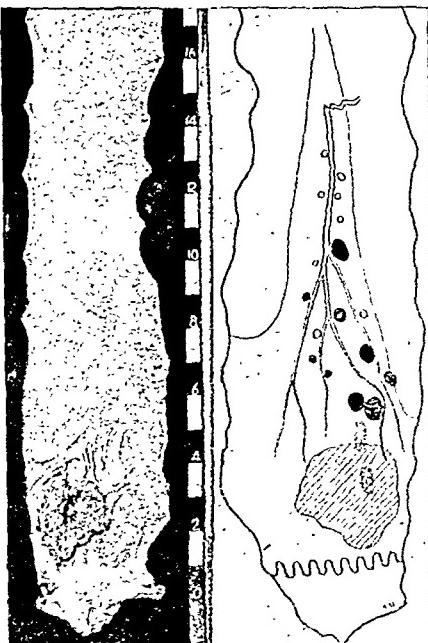
FIG. 9.

scope of perineal excision, regarding all border-line cases as better treated by a combined excision. Approaching the series of 425 cases in this way and considering each separately I found there were only 85 in which the glandular metastases were so situated that they would certainly have been included in a perineal excision, a proportion of exactly one in five. For tumours in the lower third and ampulla the proportion within the scope of perineal excision was slightly higher than for growths situated in the upper third, but the difference was slight. I do not claim that the remaining 340 cases could all have been cured only by a combined operation. They include some which might with luck have been cured by perineal excision and some which were actually beyond the scope of any operation.

The conclusion I have reached as a result of this survey of a large series of operation specimens of rectal cancer is that of the cases now being treated by a combined excision at least half (80% of those without and 20% of those with metastases) could have stood just as good a chance of cure if they had been treated by perineal excision.

The champions of the combined operation may declare that by substituting the combined for the perineal operation they have given a better chance of cure to at least half their patients. The defenders of the perineal may reply that the combined surgeon
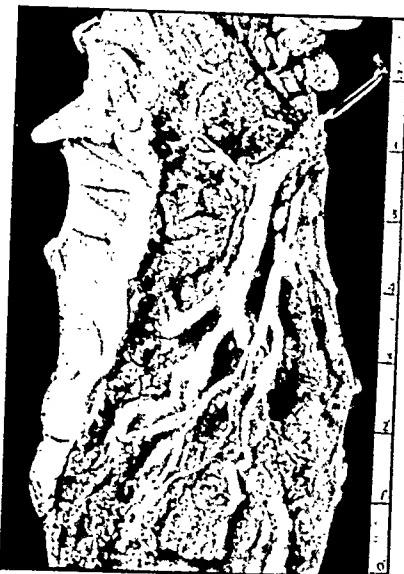
FIG. 6.—Photograph of hæmorrhoidal vein thrombosed and distended with malignant growth.

A   B   C   C1   C2
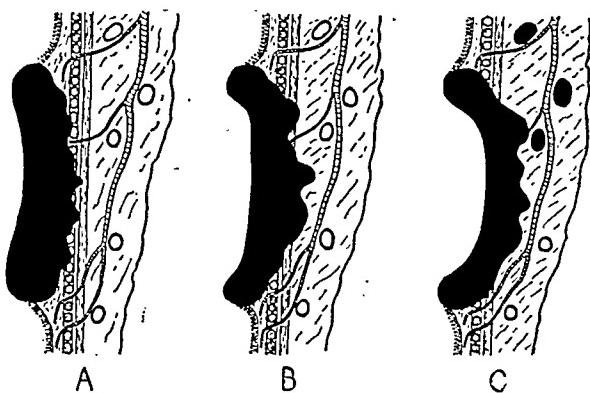
FIG. 7.—A. Growth limited to wall of rectum.
    B. Extension of growth to extra-rectal tissues, but no metastases in regional lymph nodes.
    C. Metastases in regional lymph nodes.
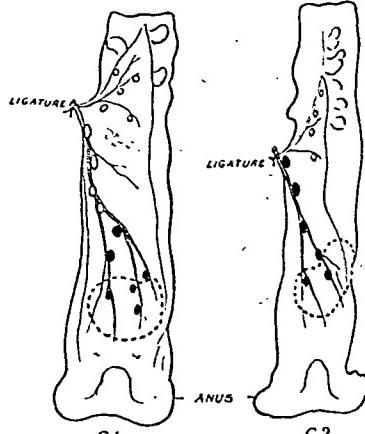
FIG. 8.—In cases labelled C 1 metastases are present in some of the lymphatic glands but the uppermost hæmorrhoidal glands are still free. In C 2 cases the lymphatic spread has extended up to and including the gland immediately below the ligature.

they could be removed by a combined operation but not by a perineal excision? Before entering this controversial field, or it might be more appropriate to say, before venturing into the lion's den, let me define the isssue as clearly as possible. It will I think be generally admitted that growths without lymphatic metastases and ampulla of the rectum have as good a chance of cure whether the ˉoperation be perineal or combined excision. The same is true of many growths situated in the upper third of the rectum, but not of all, because perineal excision cannot reach as high as combined. After a general survey of operation specimens of rectal cancer without lymphatic metastases, all removed by combined operation, I formed the impression that about 80% of these might have been treated by perineal excision with an equal chance of success.

The combined operation is manifestly superior to the perineal for most cases with

of individuals who survive each year. It will be seen from fig. 11 that after the operation of rectal excision a sharp decline in number takes place for the first two or three years, due no doubt to recurrences, after which the curve gradually straightens out. About 40% of patients were alive after five years. It must not be inferred that the 60% who did not survive all died of rectal cancer. To calculate the number of rectal cancer deaths we have to subtract the number of deaths expected in a population of similar composition as regards age and sex. The estimated survival of a control population has been calculated from the Registrar-General's Returns and is recorded by the broken line in fig. 11. A comparison of the survival of the excision of the rectum cases (continuous line) with the control population (broken line) shows that after a period of five years the survival lines run parallel. In the first place it is clear that nearly all deaths from recurrences occur during the first three years and that it must be very rare for patients who have survived the fifth anniversary of this operation to die of a recurrence. No doubt there are exceptional cases of cancer of a low grade of malignancy which run a course of more than five years and ultimately prove fatal (some cases of this sort being included in our records), but the risk of dying from rectal cancer more than five years after operation is insufficient to be detected by comparison with the control population. Secondly we learn from this chart that 60% of the rectal cancer cases were dead at the fifth anniversary and 10% of the control population had also died of other causes. By subtracting this 10% we are justified in assuming that only 50% of the deaths in the rectal excision group are actually due to rectal cancer. It is extremely rare for any untreated case of rectal cancer to survive for five years and the conclusion is obvious that the surgical treatment given to these patients cured approximately half. Finally it is interesting to notice that once the risk of recurrence has passed a patient who has been deprived of his rectum has as good an expectation of life as a person of similar age who still possesses this organ, a comforting thought for surgeons to plant in the mind of a patient hesitating about submitting to operation.

In fig. 12 the survival of rectal cancer patients treated by excision is compared with those treated by colostomy only. For the most part these latter were so treated because the malignant disease was too far advanced for there to be any prospect of cure by radical excision. The two groups of cases differed therefore in stage of development and also in respect of age and sex and so are not strictly comparable, but the expression of the facts of survival as they stand does enable comparison to be made between the fate of patients treated by colostomy only and those by radical excision. Colostomy is a grim sentence. In this series the operative mortality was 15.6% and more than half the operation survivors died within twelve months. The original population was 492 individuals, of whom three lived for five years and none survived to the sixth year.

Fig. 13 compares the survival after excision of the rectum of males and females. Rectal cancer is commoner in men than in women. On the other hand at the time of treatment the disease is generally at a more advanced stage in women than in men, there being an increase of 10% in the proportion with lymphatic metastases. These advantages and disadvantages appear to cancel themselves out at first for the survival curves of the two sexes follow a similar course for the first three or four years, after which there are more female survivors than men. The expectation of life of a control population of adult women is slightly better than that of men and it is interesting to notice that when once the risk of recurrence has passed the women cancer patients treated by rectal excision enjoy the advantage which seems to be their birthright.

It is true of cancer of all organs of the body that the results of surgical treatment could be much improved by earlier treatment. This can be shown in a very convincing way for rectal cancer by comparing the survival rate of A, B, and C cases after radical excision either by perineal or the combined operation (fig. 14). Of the A cases treated by perineal excision 82.2% were alive after five years and of those treated by combined 83.9%. For B cases also the results of surgical treatment were very satisfactory, showing a five-year survival rate of 61.2% for the perineal and 62.3% for the combined operations. Unfortunately at the present time less than half the patients are operated on at the A and B stage and once lymphatic spread has commenced the prospects of surgical cure begin to decline especially for the perineal group (C cases in fig. 14). A very considerable improvement would therefore result if a larger proportion of cases were treated before the stage of lymphatic metastases. Prompt treatment is more than ever imperative once lymphatic spread has commenced. If we take C 1 cases as representing early lymphatic spread and C 2 as late then a move forward from C 2 to C 1 would mean an improvement of 15% for the perineal group and more than twice this for the combined (fig. 15).

A comparison of the total survivors after excision of the rectum treated by perineal operation (391 patients) and combined (514 patients) shows very little difference (fig. 16).

submits about half his patients to an unnecessarily extensive operation. A better defence of the perineal operation would be to refer to the graphs illustrating the result of surgical treatment (figs. 16 and 17), or to quote the following case which shows that perineal excision may sometimes succeed even when the case seems more suitable for a combined operation.

Fig. 10 is a photograph of the operation specimen and gland dissection from a patient on whom Mr. O. V. Lloyd-Davies carried out a perineal excision in 1938. Lymphatic metastases were found along the course of the superior hæmorrhoidal vessels, but the patient made a good recovery and has remained in good health for more than five years. She has recently married in spite of her colostomy, but before having children she told me her husband wished to be reassured that they would not be born "with the back passage in front".
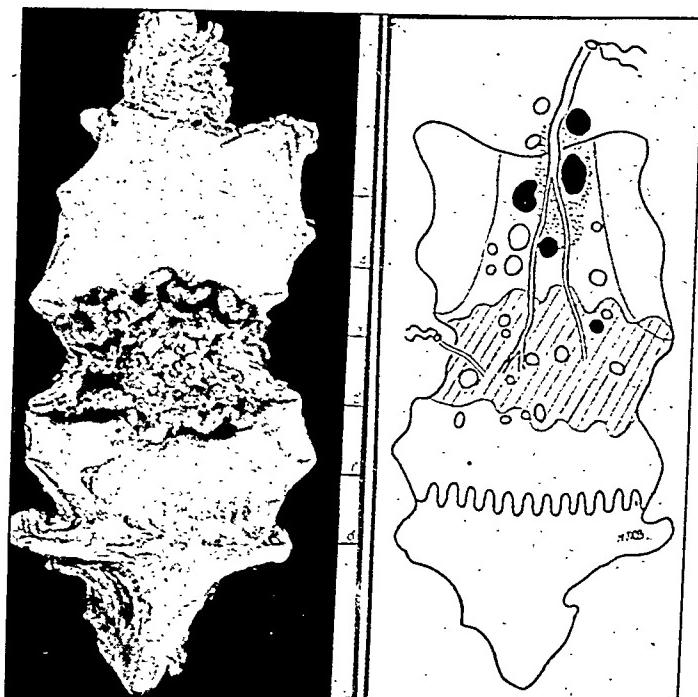
FIG. 10.—Perineal excision: five lymphatic metastases and venous invasion. Patient alive and well five years later.

RESULTS OF SURGICAL TREATMENT OF RECTAL CANCER

The cases hitherto described were exceptional in character. I choose them deliberately to show that patients with very extensive local, venous and lymphatic spread may sometimes pass the five-year milestone in defiance of all established principles of prognosis. No one can foretell what may happen to an individual patient but for a large group of cases the average expectation of life may be foretold with mathematical precision.

The charts are based on an analysis of 905 cases of rectal cancer treated by radical excision at St. Mark's Hospital (514 by combined and 391 by perineal excision) and on an additional 492 cases treated by colostomy alone. The patients were followed up year by year and only 32 of the excision cases were lost sight of, thanks to the care taken by those responsible for the records. I am greatly indebted to Mr. W. B. Gabriel, who with the help of a grant from the Medical Research Council, started this follow-up in 1922 and supervised it personally for fifteen years, and also to Mr. O. V. Lloyd-Davies who is in charge at present. These unique records are now providing information which has never before been available on such a scale.

The first chart (fig. 11) records the general survival rate of cancer of the rectum treated by radical excision. In this, and all succeeding charts, the upright axis records the number of individuals alive and the horizontal axis the time of survival in years. The initial population is represented as 100 so the graphs actually record the percentage
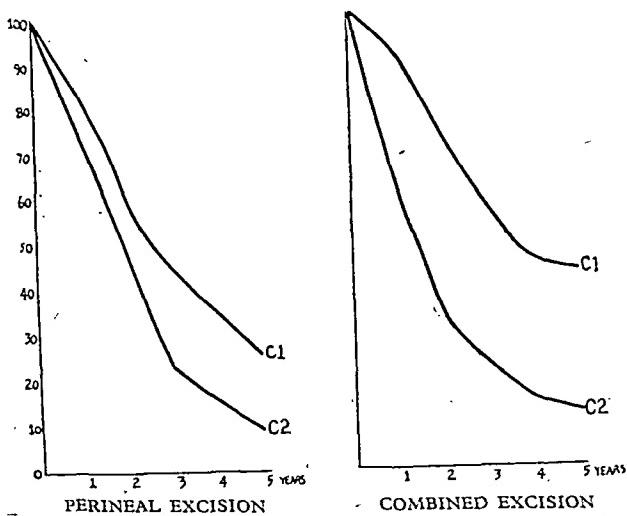
FIG. 15.—Comparison of survival rates of C1 and C2 cases. (Operation deaths excluded.)

PERINEAL EXCISION   COMBINED EXCISION

OPERATION DEATHS INCLUDED   OPERATION DEATHS EXCLUDED
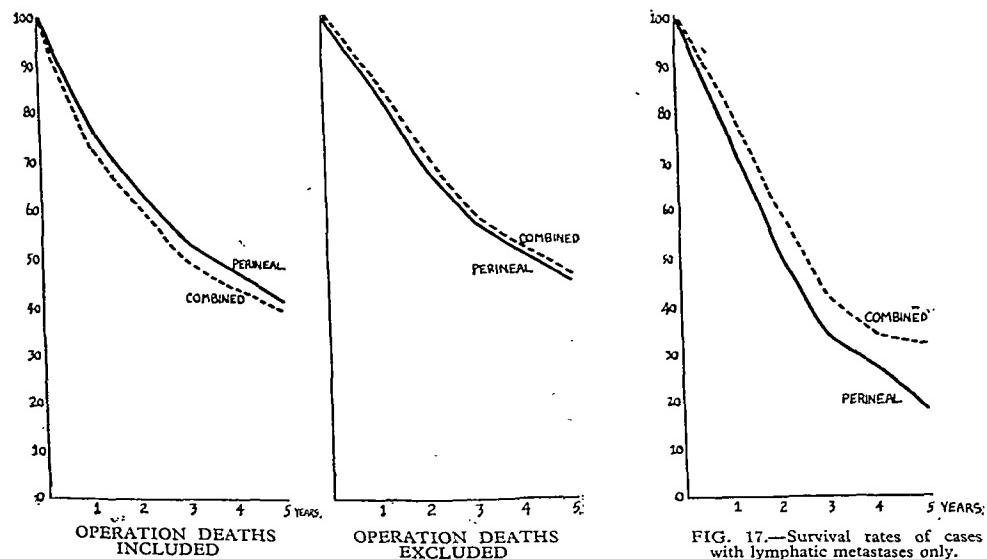
FIG. 16.—Comparison of survival rate after excision of the rectum by *perineal* (continuous line) and *combined operation* (broken line).

FIG. 17.—Survival rates of cases with lymphatic metastases only.

If the operation deaths are included then the perineal group showed 40·9% alive after five years compared with the 39·2% of survivors from the combined operations. On the other hand by excluding operation deaths and limiting the comparison to operation survivors then the combined operations could boast a slight advantage, 47·1% being alive after five years compared with 44·9% of the perineal. In this series the operative mortality of the combined operations was 15% and of the perineal 8·7%. This difference has turned the scale but is unlikely to do so in the future because the operative mortality of the combined operation is steadily declining.

There is no doubt that the combined operation because of its more extensive clearance of the lymphatic field, does cure some cases in which perineal excision could not succeed. If fig. 16 could be taken as a fair comparison then it would seem that the number of patients cured by the more extensive operation was small and did not equal the number lost through the initial higher operative mortality. Obviously survival rates of patients treated by different methods cannot be compared if the two groups
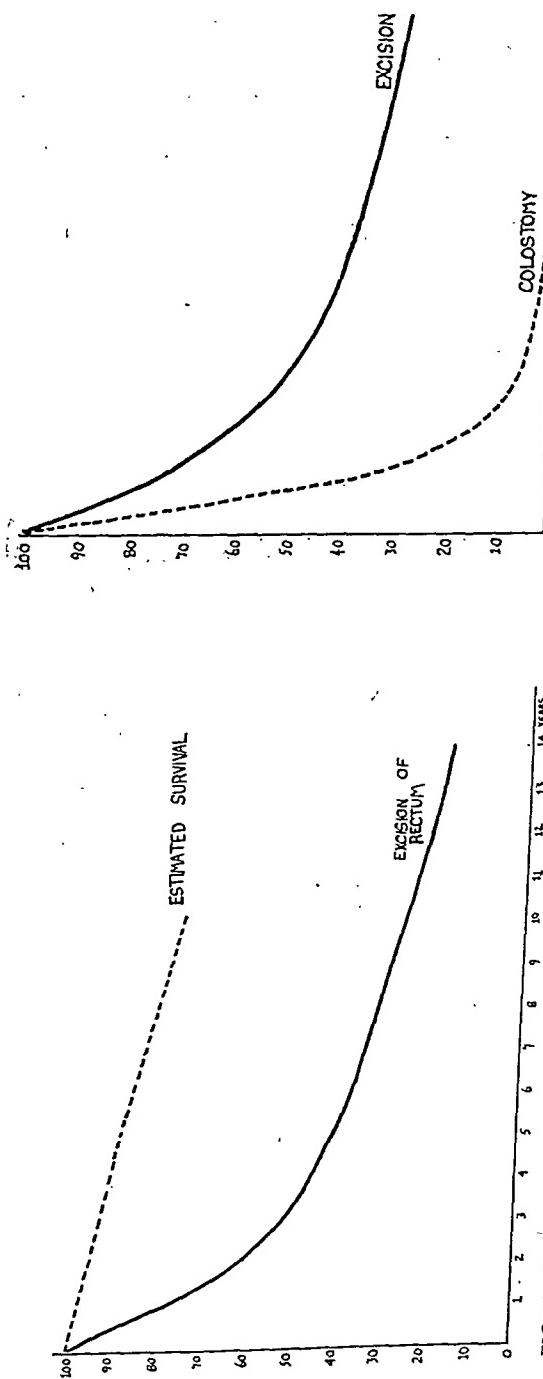
FIG. 11.—Survival rate of rectal cancer treated by excision compared with estimated survival of a control population similar in age and sex.
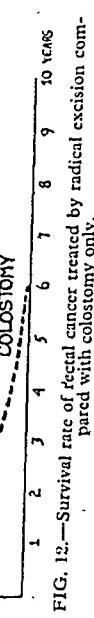
FIG. 12.—Survival rate of rectal cancer treated by radical excision compared with colostomy only.
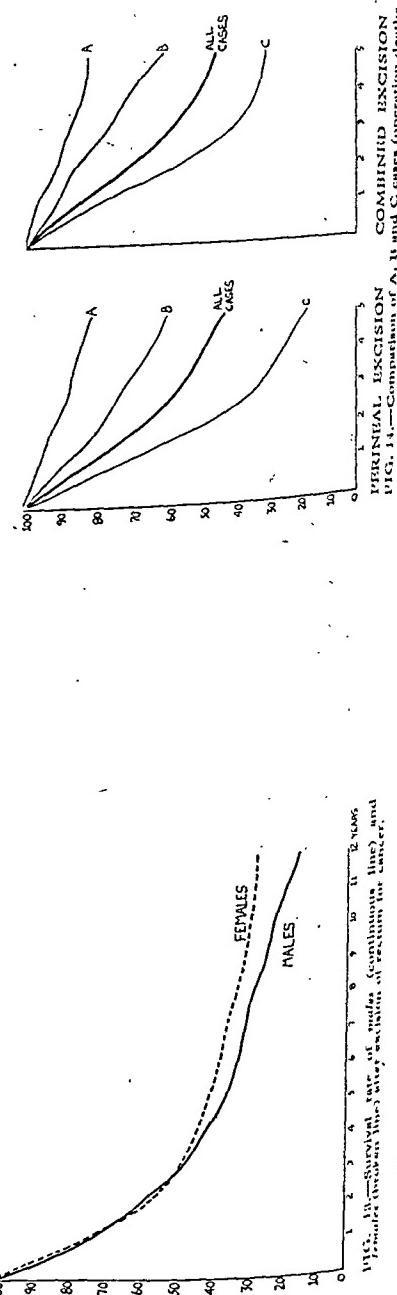
PERINEAL EXCISION

COMBINED EXCISION

FIG. 14.—Comparison of A, B and C cases (operation deaths

FIG. 13.—Survival rate of males (continuous line) and females (broken line) after excision of rectum for cancer.

Section of Anæsthetics

President—R. J. MINNITT, M.D., D.A.

[*November 5, 1943*]

Pulmonary Complications Following Simple Herniorrhaphy

By Squadron Leader B. G. B. LUCAS, R.A.F.V.R.

AN investigation was made to ascertain why the percentage of pulmonary complications following inguinal herniorrhaphy in Service cases appeared to be so high and, if possible, to reduce their number. Though most of the complications following herniorrhaphy are of a mild character, and not sufficient to interfere seriously with convalescence, yet they can make life extremely uncomfortable for the patient.

For statistical purposes I divided these post-operative chests into four groups: (1) Those who complained of a cough for the first forty-eight hours following operation but did not expectorate or have any other clinical signs except occasionally a temperature of 99° F. (2) Those who had mild clinical signs in the chest and a temperature of up to 100° F., but which cleared up within three days. (3) Those whose "chests" lasted between three and five days, and (4) Those who had a "chest" longer than five days.

All the patients were seen and examined several times following operation and the results were noted on their anæsthetic records. Often the only evidence of a cough was the patient's own statement, but as this investigation was being carried out primarily for his benefit, one felt that his word should be believed.

The type of operation was the same for all the cases under review. It was the so-called McArthur operation in which a strip of external oblique fascia is used to repair the inguinal canal. Only unilateral cases being operated upon for the first time were included. The premedication used, unless otherwise mentioned, was a third of a grain of omnopon and one hundred and fiftieth of scopolamine given one hour before operation.

The first series was operated upon under general anæsthesia using half a gramme of pentothal followed by nitrous oxide, oxygen and ether in a Boyle's apparatus. Of 85 cases 10·5% coughed, 20·0% had slight "chests", 16·5% moderate and 14·1% severe.

These figures seemed extraordinarily high. To verify the statement that ether itself is not a factor in post-operative respiratory complications (Sircar and Boston, 1940), a number of cases was done under half a gramme of pentothal followed by gas and oxygen alone. The total number of cases was 69 and the results were: 10·2% coughed; 20·3% had slight "chests"; 8·1% moderate and 8·1% again severe.

This was slightly better than the ether series, but although the number of moderate and severe "chests" was slightly reduced, that of the mild ones remained unaltered.

It was now decided to investigate the possibilities of local anæsthesia. The method chosen was a regional nerve block injected in the area between the lowest costal margin and the superior iliac crest. This, rather than infiltration near the operation site, was selected for two reasons. Local infiltration distorts the anatomy of the region and predisposes to infection. Also regional anæsthesia can be carried out by the anæsthetist and not by the surgeon, so saving time. 1% novocain was used. During the operation small doses of pentothal were given from time to time to keep the patient asleep. It was felt that local anæsthesia alone, without some heavy premedication, was not ideal from a psychological point of view, and although omnopon and scopolamine does produce some mental dullness, it does not achieve any amnesia in the great majority of cases.

Of 68 cases 13·2% coughed; 8·8% had slight "chests"; 10·2% moderate and 11·8% severe ones. This then appeared an unsatisfactory method as the results were only slightly better than those under general anæsthesia. Admittedly, the cough and mild cases were slightly less, but the number with no complications at all was roughly the same; 56% as opposed to 53%. But the number of moderate and severe chests was higher than with pentothal, gas and oxygen.

So an effort was made to find some more suitable premedication in place of the pentothal with the local so that the patient while being comfortable and, if possible, asleep and amnesic, would not be too depressed from a respiratory point of view during the operation. Various drugs were tried, but none was found to be completely satisfactory. The opiates and oral barbiturates in large doses caused too much

are dissimilar in constitution. There is ample evidence that the group of cases treated by combined operation were of a more advanced character than those treated by the perineal and no conclusion should be drawn unless allowance has been made for this handicap.

The operations analysed in this survey were carried out over a period of fifteen years. During this time many improvements in operative technique and after-care were introduced allowing surgeons to accept as suitable for excision cases which were formerly regarded as inoperable. Mr. L. E. C. Norbury, senior surgeon to St. Mark's, has pointed out that the hospital operability rate, which was 51% in 1930, rose with the more general adoption of the combined operation until it reached 71% in 1936 and it has reached a higher level since then.

The acceptance for operation of cases formerly regarded as inoperable has had as a natural consequence a striking rise in the proportion of cases found to have lymphatic metastases. Before the year 1928 our records showed lymphatic metastases in 42% of operation specimens. The proportion with metastases rose to 47% in the five-year period 1928-1932 and to 53% in the next five years. These changes did not affect equally the perineal and combined operation patients because in the years when the operability rate was low and the percentage of cases with lymphatic metastases corres- pondingly low, the majority of excisions at St. Mark's Hospital were carried out by the perineal method, whereas in more recent years when the operability rate has risen and been accompanied by a rise in the proportion of cases with lymphatic metastases, most of the excisions have been carried out by a combined operation. The bolder policy towards rectal cancer which has characterized surgical treatment in recent years has obviously adversely handicapped the score of the combined operation as compared with perineal. I am convinced that if the operability rate had not altered and the proportion of cases with lymphatic metastases had remained constant then a comparison between the two operations would have shown a more substantial margin in favour of the combined operation.

With the figures available at the present time the fairest procedure is to limit any comparison of these two operations to cases with lymphatic metastases. In cases without lymphatic metastases the survival rate is practically the same irrespective of the operation but when comparison is made of survival rates of those with lymphatic metastases (fig. 17) we see that the combined operation has a steadily increasing advantage over the perineal, reaching to 13% after five years. Having watched with admiration the improvements in surgical technique which have been introduced in recent years I venture to prophesy that the ultimate credit balance of the combined operation for cases with lymphatic metastases judged on a five-year basis may reach as much as 15 to 20% in the end.

Advances in surgical technique and the planning of operations have steadily increased the operability rate, whilst at the same time the operation mortality has been reduced by improvements in anæsthetics, by team work and more careful post-operative super- vision. The result has been that the percentage of five-year cures has steadily risen.

It should be made better known to the world at large that in its early stages rectal cancer can be completely cured and that even in its more advanced stages the results of surgical treatment are often very satisfactory. The chief need of the day is earlier diagnosis.

The following references give a description of the surgical operations mentioned:

(1) *Abdomino-perineal*: MILES, W. E. (1939) Rectal Surgery, London, p. 260.
(2) *Perineal excision*: MUMMERY, J. LOCKHART (1938) *Surg. Gynec. Obstet.*, 67, 655.
(3) *Perineo-abdominal*: GABRIEL, W. B. (1934) *Lancet* (ii), 69.
(4) *Synchronous combined*: LLOYD-DAVIES, O. V. (1939) *Lancet* (ii), 74.

diffuse variety. Similarly there was little sputum at first but when it did appear it was purulent and sometimes slightly rusty in character.

The treatment of both types of atelectasis was the same and was purely mechanical. Its aim was to expand the lungs and to promote coughing. This was done by an intensification of the breathing exercises previously mentioned and hourly administrations of carbon dioxide. Movement in bed was encouraged as far as possible.

The results of chemotherapy in the treatment of these post-operative chests have been extremely poor. This conclusion has been reached not only from a study of these cases under review but also from the observation and treatment of all the post-operative pulmonary complications following other operations over the same period of time. Although chemotherapy will lower the temperature, the other signs and symptoms remain unaltered and the average duration of the condition is more than doubled. It is difficult to explain why this should be so but possibly the toxic effect of the therapeutic drug causes a certain amount of "miserableness" on the part of the patient, with the result that the all-important stirring up of the lungs is not done properly. In all these cases of herniorrhaphy there were no examples of massive collapse of the lung and those who developed lobar atelectasis all showed signs of re-expansion and improvement within four days. But should this not be so, bronchoscopy is to be recommended. This has been adopted as the standard treatment for all other cases of lobar and massive collapse which have occurred post-operatively and have not responded to expansion therapy within five days. So far it has given very good results.

To turn now to the cause of this high incidence of post-operative pulmonary complications following herniorrhaphy. The majority of these "chests" are atelectatic in origin and this is probably the key to the problem. One very definite factor is the immediate post-operative respiratory depression due to the method of anæsthesia employed. This depression allows small plugs of mucus to settle in the bronchioles, with resulting collapse. The collapsed area subsequently becomes infected. If any respiratory infection is present obviously there will be a greater amount of mucus present than normal with a consequent increase in the possibility of the bronchioles being obstructed.

But this depression of respiration by the method of anæsthesia is not all. Early in this investigation it was noticed that most of the chest complications occurred mainly on the same side as the operation. So 14 cases were screened four hours after operation. Unfortunately, owing to the small number of cases screened and because of technical difficulties no precise results could be obtained, but in all cases there was a definite diminution in diaphragmatic movement on the operated side. Of the 14 cases, 1 developed a moderate "chest" and 3 slight. These findings have recently been confirmed by Bird, Kilner and Martin (1943).

Why was there this partial fixation of the diaphragm? Was it due to sympathetic stimulation from the spermatic cord during operation causing a spasm of the diaphragm afterwards? To prove or disprove this. in about 30 cases, some under general and others under local anæsthesia, 10 c.c. of 2% novocain was injected around the cord after exposure but before it was handled, to block any sympathetic impulses that might arise from this site. This, however, appeared to make no difference whatsoever.

One is led to the conclusion that this fixation of the diaphragm and post-operative hypoventilation are due to some common factor which is not present to the same extent in any other condition. This is undoubtedly post-operative pain at the operation site on respiration. In the operation of inguinal herniorrhaphy certain muscle layers are deliberately tightened and sewn together so that they are unable to move as freely, one with the other, as they were accustomed. Now in the male, deep respirations are always associated with the movement of all abdominal muscles. Hence there is pain on respiration, inhibiting it at a time when it is of greatest value.

This unfortunately cannot be the whole story, as it would not account for the fixation of the diaphragm before the patient recovers consciousness, but it is probably the main reason. This is borne out in two ways. Firstly, the unco-operative miserable patients who are terrified to breathe deeply because of pain get more "chests" than the others, and secondly, there is the improvement brought about by post-operative breathing exercises. The final test of this theory would be, of course, to anæsthetize the hernial area in such a way that the analgesia would last several days. If this were so there would be no post-operative pain to inhibit respiration. It could be done theoretically by using paravertebral block anæsthesia with an oily anæsthetic solution such as proctocaine. So far I have not done this as I am not convinced that the injection of large quantities of an oily solution around a nerve root is entirely free from danger.

In conclusion, I would like to touch upon the very old question of the choice of anæsthesia for inguinal herniorrhaphy. My opinion is that, all things being equal, the number of post-operative "chests" is roughly the same whatever the method, but with

respiratory depression as did avertin or pentothal rectally, while oral barbiturates in small doses often caused excitement. Eventually chloral hydrate was chosen as it had less respiratory depression than any other drug, and with omnopon and scopolamine produced very good amnesia. Two doses of thirty grains were given; one the night before and the other three hours before operation.

The first series done with this method showed somewhat similar results to those of pentothal and local. Of 46 patients 17·4% coughed; 13·4% had mild "chests"; 2·9% moderate, and 10·9% severe. But it was thought that these results might be improved if the patients could fully ventilate their lungs immediately following operation. Accordingly a system of pre- and post-operative breathing exercises was instituted. These aimed at expanding the bases of the lungs, being modified from those originally described by MacMahon (1928). They were taught to the patient the day, or if possible several days, before operation and his co-operation was obtained as far as possible. Immediately on returning from the operating theatre the exercises were begun, and repeated under supervision every four hours, or more often, for the first forty-eight hours, and afterwards twice daily with the addition of abdominal and leg exercises to maintain the general tone of the muscles of the body.

This method has so far given the best results, and has effected a reduction in the number of post-operative respiratory complications. Total number of cases 87. Of these 11·2% coughed; 6·9% had mild "chests"; 6·9% moderate, and 6·0% severe.

Spinal anæsthesia was not used at all for any series of cases as it was considered that the post-operative complications such as headache, backache, &c., would outweigh any advantages there might be in the case of its administration. Also, the general opinion at present is that the respiratory complications of spinal anæsthesia are as high if not higher than those which follow any other form of anæsthesia.

When all the cases of post-operative pulmonary complications were analysed from a clinical point of view they were found to be of three main types. The first were the simple coughs. These were difficult to identify accurately as they had no clinical or radiological signs beyond the occasional temperature. These cases all cleared up rapidly without any special treatment.

Secondly, there were the cases of simple bronchitis. These all showed the typical signs and symptoms of that disease with cough, temperature of 100° to 101° and slightly raised pulse and respiration rates. The condition lasted about a week or so, and, as was to be expected, was more common in the older patients. Standard medical treatment, such as inhalation and expectorant mixtures, was found to give the best results for this group of cases.

The remaining group of post-operative "chests" constituted the great majority. They were all cases of atelectasis and could be subdivided into two types, diffuse and lobar. Diffuse atelectasis was the more common. The condition first gave rise to symptoms about thirty-six hours following operation when there was a dry cough and a temperature of 99° to 101°. The pulse and respiration rates were both raised and the patient might complain of a vague tightness of the chest. At this stage there were often no clinical signs, but occasionally the breath sounds might be slightly diminished at both bases or a few scattered crepitant râles might be heard. Twenty-four hours later the temperature was still raised and sputum appeared. This was thick and rapidly became purulent. On auscultation many fine râles could be heard in all areas. In the more severe types small patches of what appeared to be consolidation were sometimes detected. At this stage there was usually some dyspnœa.

Radiologically the picture was somewhat confusing, depending at what stage the X-ray was taken. If it was taken very early, within four to eight hours of the onset, minute areas of collapse could be seen scattered throughout the lungs. This picture was very similar to that of the pneumonitis of young children described by Gill (1938). But in the great majority of cases this was only transient and an X-ray taken eight hours later revealed absolutely nothing. The duration of the condition varied but a straightforward case with suitable treatment usually cleared up within four or five days, the temperature resolving rapidly. One has formed a very definite clinical impression that those cases which occurred following operation under general anæsthesia, particularly with ether, were more severe in character and lasted longer.

Lobar atelectasis occurred less frequently but was a more severe condition. The onset was similar to that of the diffuse variety but pain and dyspnœa were more marked. Often there was some cyanosis. Examination of the chest revealed all the signs of collapsed lobe with diminished movement, dullness and diminished or absent breath sounds. As one would expect, only the middle and lower lobes were affected, often on the same side as the operation. Radiography confirmed these findings. The temperature rose for the first twenty-four to thirty-six hours up to 102° or 103° and then resolved rapidly like the

inhalation anæsthesia, particularly using ether, the "chests" are more severe. This is what one would expect as any lung tissue which may collapse, instead of being normal and healthy to start with, has been grossly irritated by the ether. This predisposes to infection. I believe that the advantage of local anæsthesia lies in the fact that post-operative hyperventilation can be carried out immediately on return from the operating theatre, so combating this period of post-operative respiratory depression which is so harmful from a chest point of view.

REFERENCES
BIRD, H. M., KILNER, S. D., and MARTIN, D. J. (1943) *Brit. med. J.* (i), 754.
GILL, A. MORTON (1938) *Brit. med. J.*, (i), 501.
MacMAHON, C. (1928) *St. Bart's Hosp. Rep.*, 61, 81.
SIRCAR, B. N., and BOSTON, F. K. (1910) *Brit. med. J.* (ii), 82.

Mr. Derrick J. Martin referred to the investigation he, with others, had carried out at an E.M.S. Hospital on 2,000 consecutive operations on Service cases. In the main, his findings were in agreement with those of Squadron Leader Lucas. He showed that the site of operation was the most important factor, quoting the results following herniotomy and Trendelenburg operations. These two operations took the same time (average twenty-seven minutes) and similar depths of anæsthesia. Hernial repairs showed a complication rate of 45% and Trendelenburg operations 1%.

In order to encourage deep breathing he had made a habit of getting all the hernio-tomies up after twenty-four hours as it was found that patients could then breathe more deeply than in bed and could cough with less pain through the support afforded to the inguinal canal by the thighs. This did not lessen the incidence of complication but lessened its length and severity.

Surgeon Lieutenant-Commander T. F. Miles: In a series of 218 operations for repair of inguinal hernia in male Service patients no records have been kept for minor coughs and these observations are necessarily confined to the 20 cases of atelectasis which occurred and which were diagnosed clinically and confirmed radiologically. These would fall among the moderate and severe cases in Squadron Leader Lucas's analysis. This incidence is higher than in a smaller series of other lower abdominal operations, mostly appendicectomies, and is in marked contrast to over 1,000 orthopædic and neurosurgical operations, which have been performed during the same period with rarely even a slight cough arising therefrom.

The more extensive Gallie operation would appear to carry a greater risk of atelectasis, as 13 cases occurred following 82 Gallie operations, whereas 5 occurred following 114 Bassini operations.

A series with ether anæsthesia and another with cyclopropane show a slight advantage for the latter, but the numbers are too small and the difference too slight to be conclusive. On the other hand the choice of anæsthetist may be important as in this series the risk of atelectasis was three and a half times greater with "conscripted" anæsthetists than with regular anæsthetists. It is probable that the occasional anæsthetist gets his patient too deep so that there is delayed recovery and a longer period of shallow breathing.

Atelectasis, being a mechanical rather than an inflammatory condition, is not neces-sarily more frequent during the winter months. From October to March there were 5 cases after 74 herniotomies, while in the following period, April to September, there were 8 following 75 herniotomies, 3 occurred towards the end of June when a minor heat wave was noted.

In this series 28 herniotomies were performed on men over 40 with one case of atelectasis. Over half had chronic bronchitis and mostly Gallies were performed. It seems that younger men, owing to pain, are more frightened to breathe deeply.

The incidence of chest complications can be lowered by skilful nursing, entailing moving the patient about in the bed, deep breathing exercises before and after operation, and the avoidance of morphia post-operatively.

Major R. J. Clausen, R.A.M.C., said that at the military hospital where he was stationed 414 operations for hernia were done during the period January to October 1943 inclusive, and from them he had records of only 53 chest complications, or 13%. It was clear that the criteria of complications were much less stringent than those of Squadron Leader Lucas.

Of these operations 164 were done under spinal anæsthesia and had 12 complications. 175 were done under pentothal-gas-oxygen, with 29 complications. 29 with pentothal-gas-oxygen-ether had 7 complications, and 31 with gas-oxygen-ether alone had 5 complica-tions. Insignificantly small groups had other anæsthetics.

He had been impressed by the prevalence of coughs and colds among soldiers, who, when histories were being taken, often said: "Yes, just the usual cough"; or "The usual soldier's cough", and so on. It seemed that soldiers were by nature prone to catarrhal infections of the respiratory tract, and this might be attributable to their mode of life, which tended to alternate between crowded stuffy rooms and exposure out of doors. In view of this catarrhal tendency he agreed with Dr. Massey Dawkins in condemning tracheal intubation.

Another point of interest on which he hoped someone would be able to give statistics was the relation of smoking to chest complications, for many officers and other ranks were heavy smokers. He did not think it was any use to stop smoking for a few days before operation, as was often recommended; if the abstention was for a few months, it might be of value.

inhalation anæsthesia, particularly using ether, the "chests" are more severe. This is what one would expect as any lung tissue which may collapse, instead of being normal and healthy to start with, has been grossly irritated by the ether. This predisposes to infection.   I believe that the advantage of local anæsthesia lies in the fact that post-operative hyperventilation can be carried out immediately on return from the operating theatre, so combating this period of post-operative respiratory depression which is so harmful from a chest point of view.

REFERENCES

BIRD, H. M., KILNER, S. D., and MARTIN, D. J. (1943) *Brit. med. J.* (i), 754.
GILL, A. MORTON (1938) *Brit. med. J.*, (i), 504.
MacMAHON, C. (1928) *St. Bart's Hosp. Rep.*, **61**, 81.
SIRCAR, B. N., and BOSTON, F. K. (1940) *Brit. med. J.* (ii), 82.

Mr. Derrick J. Martin referred to the investigation he, with others, had carried out at an E.M.S. Hospital on 2,000 consecutive operations on Service cases.   In the main, his findings were in agreement with those of Squadron Leader Lucas. He showed that the site of operation was the most important factor, quoting the results following herniotomy and Trendelenburg operations. These two operations took the same time (average twenty-seven minutes) and similar depths of anæsthesia. Hernial repairs showed a complication rate of 45% and Trendelenburg operations 1%.

In order to encourage deep breathing he had made a habit of getting all the herniotomies up after twenty-four hours as it was found that patients could then breathe more deeply than in bed and could cough with less pain through the support afforded to the inguinal canal by the thighs. This did not lessen the incidence of complication but lessened its length and severity.

Surgeon Lieutenant-Commander T. F. Miles: In a series of 218 operations for repair of inguinal hernia in male Service patients no records have been kept for minor coughs and these observations are necessarily confined to the 20 cases of atelectasis which occurred and which were diagnosed clinically and confirmed radiologically. These would fall among the moderate and severe cases in Squadron Leader Lucas's analysis. This incidence is higher than in a smaller series of other lower abdominal operations, mostly appendicectomies, and is in marked contrast to over 1,000 orthopædic and neurosurgical operations, which have been performed during the same period with rarely even a slight cough arising therefrom.

The more extensive Gallie operation would appear to carry a greater risk of atelectasis, as 13 cases occurred following 82 Gallie operations, whereas 5 occurred following 114 Bassini operations.

A series with ether anæsthesia and another with cyclopropane show a slight advantage for the latter, but the numbers are too small and the difference too slight to be conclusive. On the other hand the choice of anæsthetist may be important as in this series the risk of atelectasis was three and a half times greater with "conscripted" anæsthetists than with regular anæsthetists. It is probable that the occasional anæsthetist gets his patient too deep so that there is delayed recovery and a longer period of shallow breathing.

Atelectasis, being a mechanical rather than an inflammatory condition, is not necessarily more frequent during the winter months. From October to March there were 5 cases after 74 herniotomies, while in the following period, April to September, there were 8 following 75 herniotomies, 3 occurred towards the end of June when a minor heat wave was noted.

In this series 28 herniotomies were performed on men over 40 with one case of atelectasis. Over half had chronic bronchitis and mostly Gallies were performed. It seems that younger men, owing to pain, are more frightened to breathe deeply.

The incidence of chest complications can be lowered by skilful nursing, entailing moving the patient about in the bed, deep breathing exercises before and after operation, and the avoidance of morphia post-operatively.

Major R. J. Clausen, R.A.M.C., said that at the military hospital where he was stationed 414 operations for hernia were done during the period January to October 1943 inclusive, and from them he had records of only 53 chest complications, or 13%. It was clear that the criteria of complications were much less stringent than those of Squadron Leader Lucas.

Of these operations 164 were done under spinal anæsthesia and had 12 complications. 175 were done under pentothal-gas-oxygen, with 29 complications, 29 with pentothal-gas-oxygen-ether had 7 complications, and 31 with gas-oxygen-ether alone had 5 complications.   Insignificantly small groups had other anæsthetics.

He had been impressed by the prevalence of coughs and colds among soldiers, who, when histories were being taken, often said: "Yes, just the usual cough"; or "The usual soldier's cough", and so on. It seemed that soldiers were by nature prone to catarrhal infections of the respiratory tract, and this might be attributable to their mode of life, which tended to alternate between crowded stuffy rooms and exposure out of doors. In view of this catarrhal tendency he agreed with Dr. Massey Dawkins in condemning tracheal intubation.

Another point of interest on which he hoped someone would be able to give statistics was the relation of smoking to chest complications, for many officers and other ranks were heavy smokers. He did not think it was any use to stop smoking for a few days before operation, as was often recommended; if the abstention was for a few months, it might be of value.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*October 21, 1943, continued*]

Dermatomyositis With Sclerodermatous Onset.—HUGH GORDON, M.C., M.B.

S. W., aged 60.

The patient, a previously healthy man, noted twelve months ago chafing on his insteps, which he attributed to rubber boots. The skin became irritated and sore, no doubt partially due to irritant applications which he applied himself, and the condition was described as spreading up to his knees. The legs became stiff and walking was interfered with.

Three months ago irritation and redness were noticed on the back of the left forearm. This spread up both forearms and the hands were noticed to become swollen. He presented himself for advice a few days previously.

On examination.—A dusky red, sclerodermatous condition of both forearms and lower limbs. The skin of the lower limbs is atrophic and in places broken. There is marked shrinking, which appears to be real, of the muscles of the forearms.

A tentative diagnosis of dermatomyositis with sclerodermatous onset has been made.

A section from the forearm showed changes in the skin and muscle consistent with the diagnosis of dermatomyositis. Routine physical examination is negative—chemical investigations negative. In view of one success in the past with sulphanilamide (40 gr. total dose), this treatment is being given to the patient.

Dr. G. B. Dowling: I agree, of course, with Dr. Gordon's view of the case, but whether it is called dermatomyositis or progressive scleroderma is, I think, immaterial, the two representing, according to my belief, different aspects of the same process.

Dr. F. Parkes Weber: I have seen a good many cases more or less like this. I think that there is very little doubt that about twenty years ago such a case would have been diagnosed as one of symmetrical generalized scleroderma of the sclerodactylia type. I agree now with Dr. Dowling that a case like the present one is to be regarded as a variety of dermatomyositis. The prognosis in the "hypertrophic" cases is better than in the atrophic.

Lipoid Necrobiosis Without Diabetes.—H. J. WALLACE, M.R.C.P.

Mrs. E. B., aged 19.

Six months ago she had two ulcers on the left leg and one on the right leg, each about ½ in. in diameter; each had been preceded by a bulla. A tentative diagnosis of staphylococcal infection was made but the picture rapidly changed, and the small ulceration was succeeded by spreading scaly areas. The centre of these lesions assumed a violaceous tint, whilst the spreading margins were brown. A little later small yellow deposits could be observed towards the periphery of each lesion and in the centre a few telangiectatic vessels developed. Each area reached its maximum size in about two months from the first appearance of any abnormality.

The size of the lesions has not altered materially in the past four months and all areas are now regressing. The general appearance was thought to resemble either the morphœa-like tuberculides or lipoid necrobiosis. Nothing relevant was elicited in the patient's past or family history, e.g. of tuberculosis. There was no evidence of local or general vascular disease.

Section showed: "Necrobiotic areas in the corium each of which were surrounded by inflammatory cells. Some dilatation of superficial capillaries. Fat could be demonstrated in these areas in frozen sections."

Mantoux negative in 1:1,000, positive in 1:100. Wassermann negative. X-ray of chest: No abnormalities seen. Blood cholesterol 130 mg.%. Noon blood sugar 0·081 %. Twenty-four hourly urine save: Sugar negative (Benedict). Albumin negative. Inoculation of biopsy material into a guinea-pig was negative for tuberculosis.

[*November* 18, 1943]

Pseudoxanthoma Elasticum ("Dermatolysis", Alibert).—J. E. M. WIGLEY, M.B., and W. FREUDENTHAL, M.D. (Previously shown Section of Dermatology, February 18, 1943; *Proceedings*, April 1943, 36, 294.)

Dr. W. Freudenthal: Two biopsies, one from the loose skin folds over the abdomen, the other from the "peau d'orange" skin above the breast; both show a widespread degeneration of the elastic tissue as found in pseudoxanthoma elasticum (elastorrhexis

Loose folds of skin over the abdomen.　　　　　　　Showing area of " peau d'orange."

Pseudoxanthoma elasticum. Broken-up elastic fibres encrusted with calcium salts. The shallow depression of the epidermis (centre) corresponds clinically to a " groove " of the peau d'orange skin.　× 35.

and elastoclasis). Furthermore, when stained for calcium by von Kossa's silver nitrate method (without staining for elastic tissue), these broken-up elastic fibres are seen to be encrusted with calcium salts. The picture thus produced is strikingly similar to

that in R. E. Wright and W. Freudenthal's case of pseudoxanthoma (Section of Dermatology, January 21, 1943; *Proceedings*, April 1943, 36, 290; *see* illustration p. 291).

Clinically the following points are of interest: (1) Some looseness or folding of the skin is very frequent in pseudoxanthoma (Brain, 1937) "abdominal skin very loose", but this excessive amount is rare, e.g. Hallopeau and Lafitte (1903), "La peau . . . rétombe comme un tablier au-devant de l'ombilic". (2) "Peau d'orange" skin (Goldsmith, 1943): Patient states that this alteration was present since early childhood, though the folds developed only fairly recently. Similar changes have been noted in some cases, Milian and Lambert (1926), "Peau citréine"; Griffith and Klauder (1943), "swine skin". (3) No discrete papules are present; they all seem to have become confluent, forming large sheets. (4) There is little difference in colour between the normal skin and that of the affected areas. The abdominal region is slightly more pinkish, breast and neck slightly more whitish than the normal skin. The absence of papules and the lack of yellowish discoloration made the diagnosis of pseudoxanthoma difficult or even impossible, without histological examination.

Further investigations.—No angioid streaks (Mr. H. Neame). No Bence-Jones albuminuria. No evidence of thyroid dysfunction. Pituitary fossa: X-rays revealed no abnormality. Chest: Opacity right apex, almost certainly a tuberculous lesion. No physical signs or symptoms (Dr. A. Morland).

REFERENCES

BRAIN, R. T. (1937) *Proc. R. Soc. Med.*, 30, 199.
GOLDSMITH, W. N. (1943) *Proc. R. Soc. Med.*, 36, 295.
GRIFFITH, G. C., and KLAUDER, J. V. (1943) *Arch. Derm. Syph.*, *Chicago*, 47, 441.
HALLOPEAU and LAFITTE (1903) *Ann. Derm. Syph.*, *Paris*, 4, 695.
MILIAN and LAMBERT (1926) *Bull. Soc. franc. Derm. Syph.*, 33, 466.

Dr. F. Parkes Weber: One thinks of other possible causes for such folds of dermatolysis. I remember a case shown here a few years ago which was accompanied by darkening of the skin. The folds in that case were about the groin. It had been suggested that the pigmentation was of the nature of acanthosis nigricans.

Dr. Louis Forman: I think the case to which Dr. Parkes Weber refers was that of an old lady (shown at the meeting 21.10.37) with a gross thickening and pigmentation of the skin. The differential diagnosis was between mycosis fungoides, acanthosis nigricans and prurigo. I have not had any subsequent information.

Dr. W. Freudenthal: Tuberculosis of the lung has been recorded in a number of cases of pseudoxanthoma elasticum. This may be more than a mere coincidence, if one remembers that the lung is an eminently elastic organ.

Circinate Sarcoid.—J. E. M. WIGLEY, M.B.

Mrs. E. D., aged 40. Two and a half years' history of slowly spreading eruption on the forehead. No symptoms, and feels perfectly well. Extending from the hair margin on to the forehead are three separate, roughly oval lines of brownish-coloured infiltration. The skin enclosed within these lines is white, shiny, and slightly atrophic. Glass pressure on the lines shows brownish infiltration but no definite lupus nodules.

General physical examination and X-ray examination of the bones of the hands showed no abnormality. Wassermann and Kahn reactions negative.

Biopsy.—In the pars papillaris and upper third of the pars reticularis there are numerous small foci of closely packed endothelial cells among which there are many multinucleated cells, surrounded by an incomplete and very narrow zone of lymphoid cells. Sarcoid.

Nodular Leprosy.—J. E. M. WIGLEY, M.B.

Male, aged 25, a Cypriot. Waiter. Has lived in England for eight years.

Treated successfully for secondary syphilis about two years ago. W.R. still positive. Has noticed some changes in his face and indefinite attacks of shivering and pains for about eighteen months.

On examination.—Leonine facies, showing groups of infiltrated nodules about the forehead, naso-labial, and malar regions, chin and lips. Loss of outer half of eyebrows. Scattered nodules on arms and trunk. Large mass in right inguinal region. Extensive yellowish infiltrated areas over the upper part of the trunk, back and front. No obvious areas of anæsthesia.

Acid-fast bacilli were found in a swab taken from his nose as well as in the granulomatous infiltration shown on section.

The President: This is a very typical case of nodular leprosy and the slides show an enormous number of Hansen's bacilli. Leprosy is not a notifiable disease in this country and no one can legally compel the patient to do anything about it.

[*November* 18, 1943]

Pseudoxanthoma Elasticum ("Dermatolysis", Alibert).—J. E. M. WIGLEY, M.B., and W. FREUDENTHAL, M.D. (Previously shown Section of Dermatology, February 18, 1943; *Proceedings*, April 1943, 36, 294.)

Dr. W. Freudenthal: Two biopsies, one from the loose skin folds over the abdomen, the other from the "peau d'orange" skin above the breast; both show a widespread degeneration of the elastic tissue as found in pseudoxanthoma elasticum (elastorrhexis

Loose folds of skin over the abdomen.

Showing area of " peau d'orange."

Pseudoxanthoma elasticum. Broken-up elastic fibres encrusted with calcium salts. The shallow depression of the epidermis (centre) corresponds clinically to a " groove " of the peau d'orange skin. × 35.

and elastoclasis). Furthermore, when stained for calcium by von Kossa's silver nitrate method (without staining for elastic tissue), these broken-up elastic fibres are seen to be encrusted with calcium salts. The picture thus produced is strikingly similar to

? Pemphigus Foliaceus.—LOUIS FORMAN, M.D.

C. B., male, aged 35.

First seen 23.9.43 when the condition had been present five weeks. It had begun on the chest and back and generalized in two weeks. General health good. No glandular or splenic enlargement. Generalized, bright erythrodermia of the trunk, face, limbs, feet and hands. The skin of the trunk was hyperkeratotic with much scaling. Numerous small areas of white skin, ? normal skin, were to be seen on the trunk. Nikolsky's sign positive on one occasion, negative subsequently.

Section from back.—There are numerous blisters beneath horny layer to be seen, and one in the deepest part of the epidermis. A few foci of infiltration in the cutis, but not of typical cellular significance. Some degree of acanthosis.

The President: When I first saw the case I thought it was pityriasis rubra pilaris, but these sections showing the blisters are rather suggestive of pemphigus foliaceus.

Lipodystrophia Progressiva.—C. H. WHITTLE, M.D.

D. C., a married woman, aged 36.

Six years' history of swelling of legs. The legs have become steadily thickened, the natural shape lost and the face and neck at the same time have got thinner and she now has a drawn cadaverous expression. Her face very strikingly resembles the face of another woman with the same condition under my care about six years ago (seen also by Dr. Parkes Weber). A photograph taken some years ago shows the change in this patient.

The legs besides their swollen appearance are cyanotic. The swelling is probably due to deposit of fat. Investigations have included basal metabolic rate, serum calcium and phosphorus, X-rays of the humerus, tibia and fibula: all normal. The suggestion of possible association with parathyroid tumour is not therefore supported in this case.

There were mental disturbances in my first case, chiefly depression. This patient also shows an anxious nervous disposition and has been recently under treatment by a psychiatrist.

No treatment is known to be of any value for the condition.

Dr. F. Parkes Weber: I have seen several examples of this so-called "lipodystrophia progressiva" since I brought forward a case at the Neurological Section of this Society (*Proceedings*, 1913, 6, 71). I would point out that the present patient shows some œdema resulting from chronic hypostatic congestion in addition to the accumulation of fat in the lower extremities. That is likely to happen in many cases, especially when there are slight varicose veins. The question arises whether atypical cases with an enormous accumulation of fat about the pelvis and thighs may be seen without the very striking fat atrophy of the face. The cases which I have seen in boys have not shown any special increase of fat in the lower part of the trunk and thighs.

Dr. E. W. Prosser Thomas: I had a woman patient of about 60 in whom the skin of the lower abdomen, buttocks, thighs, legs, and (to a lesser extent) of the extensor surface of the arms hung in large flabby folds. The face and upper part of the trunk were relatively unaffected. Her skin had apparently always been like this. I do not know whether her condition is due to an accumulation of fat in these areas or to a loosening of the skin and subcutaneous tissue of the "dermatolysis" class. Section merely showed an excess of fat.

Comedones in an Unusual Position.—C. H. WHITTLE, M.D.

W. H., a soldier aged 20.

Nine months' history of small nodules on penis. Much complaint of itching and pain which "hinders his work".

A seborrhœic subject with a scurfy scalp and scars of boils on his neck.

The Pathological Department, Radcliffe Infirmary, reported "inclusion dermoid" on a biopsy taken at Dr. Carleton's request.

This is a soldier I saw a week ago about whom his Medical Officer was worried. The lesions are on the penis. They are in three grades: (1) An exaggeration of the comedones that one does see quite frequently, and which may be said to come within the normal, but in this case one can express sebaceous material from the follicle; (2) yellowish brown follicular papules about 2 mm. in diameter; (3) rather large inflammatory papules on the prepuce.

There is a difference of opinion regarding the histology. A biopsy had been done by the pathologist at Oxford, who stated it was an inclusion dermoid. Clinically, I think the lesions are all follicular, but the section can be interpreted as either an inclusion dermoid or a comedo.—(Section shown by courtesy of Dr. Alice Carleton).

Brigadier R. M. B. Mackenna: Is the incidence of leprosy in Cyprus abnormally high, or is it merely a coincidence that this is the second leper from Cyprus who has been brought to my notice in England within a few months?

Dr. J. E. M. Wigley, in reply to Dr. Parkes Weber: MacLeod ("Diseases of the Skin", 1920, p. 498) writes of a case "of a boy in Ireland who was infected by his father, a leper from Russia resident in Ireland". He quotes (p. 505) Bensen (*Dub. Med. Journ.*, 1877) writing of the case of an Irishman who "acquired the disease in the West Indies, returned to Ireland, and communicated it to a brother who lived in close association with him and was said to have slept in the same bed".

Occupational Melanoderma.—G. B. Dowling, M.D.

Mrs. E. L., aged 44. Noticed, about three years ago, some pigmentation confined to the chin. Two and a half years ago she began work as a capstan operator, and she has been doing this work continuously up to the present. During this period she has developed a gradually deepening pigmentation of the face, forehead and neck, and on the forearms and arms, particularly on their extensor aspects. As far as she can remember, the sides of the face were first affected, the other areas being attacked somewhat later. At the same time, the surface of the sides of the face, the forehead, and the extensor aspect of the forearms has been rough.

There has never been any question of saturation of the clothes or skin with oil, as it has not been considered necessary, as it sometimes is, to wear protective rubber aprons at work.

On examination.—The forehead, face and neck are quite deeply pigmented, the colour being a slaty grey and studded with white flecks, like an arsenical pigmentation. The pigmentation is mottled, and at its periphery on the neck it is disposed in small streaks. On the forearms the colour is the same, the extensor aspect being especially involved, while on the upper arms the pigmentation is less deep and, as on the neck, reticular. It reaches the level to which the sleeves are rolled up. On the sides of the face, the forehead, and the extensor aspect of the foreams, the skin is rough, giving the impression of a rasp to touch. The reason for this is found on the forearm in a follicular hyperkeratosis, like lichen pilaris. On the backs of the fingers where there is no pigmentation, the same follicular keratosis is seen. There are a few spots of the acne type on each forearm.

The appearances in this case seem to correspond to those of a professional melanosis, and the cause is probably oil. Only the exposed parts have been attacked. As oil has never sprayed on to the skin, as it does when some types of capstans are being operated, it must be supposed that finely divided particles of the oil in the atmosphere must be responsible. I doubt whether light has played any important part in its development, since pigmentation has developed progressively through both winter and summer, and it has not been more marked during the summer.

I do not know what oil has been used.

It is the first case of the kind that I have seen, and in view of the fact that other effects of exposure to oil, notably oil acne, have been extremely common during the war, it would appear that there must be some personal factor in this case.

Dr. F. Parkes Weber: I think this is a case of occupational melanoderma. Civatte's poikilodermia as far as I know it, does not resemble this occupational melanoderma. But I am puzzled by having heard that Civatte's poikilodermia has been claimed as being due to the same oily causes as occupational melanodermas.

Dr. W. N. Goldsmith: Habermann concluded that occupational melanosis was produced not by direct exogenous action of tar and petroleum products but through inhalation, partly because it also appeared on covered parts of the body where there was any friction, and partly because the neighbourhood of hair-follicles was spared. We are also familiar with the fact that the face is the part that so often gets an ordinary auto-sensitization eczema secondary to a "washerwoman's dermatitis" and at any time of the year. Presumably in such cases it is exposure to changes of temperature and light that determines the area, or the fact that the blood-vessels there are already partly damaged and dilated. Civatte (1933, personal communication) identified his poikilodermia with the first cases of Riehl, but felt sure that his cases, and probably several of Riehl's, were not due to tar.

The President: Does Civatte's poikilodermia ever affect the forearm? A number of cases of pigmentation of the face, neck and forearms were described in Buenos Aires in 1941 (summarized in *Year Book of Dermatology and Syphilology*, Chicago, 1941, pp. 504-514). They were all ascribed either to oils or to aniline dyes in cosmetics.

Dr. Louis Forman: I showed a case at this section on July 2, 1943, of a woman with melanosis of the face and neck. She was working in a badly ventilated room, handling wigs which had been cleaned with benzolene. I suggested that the ventilation should be improved and I believe the pigmentation has now become much less. In that case, the pigmentation was more marked in the folds of the chin and neck, suggesting an external irritant.

? Pemphigus Foliaceus.—Louis FORMAN, M.D.

C. B., male, aged 35.

First seen 23.9.43 when the condition had been present five weeks. It had begun on the chest and back and generalized in two weeks. General health good. No glandular or splenic enlargement. Generalized, bright erythrodermia of the trunk, face, limbs, feet and hands. The skin of the trunk was hyperkeratotic with much scaling. Numerous small areas of white skin, ? normal skin, were to be seen on the trunk. Nikolsky's sign positive on one occasion, negative subsequently.

Section from back.—There are numerous blisters beneath horny layer to be seen, and one in the deepest part of the epidermis. A few foci of infiltration in the cutis, but not of typical cellular significance. Some degree of acanthosis.

The President: When I first saw the case I thought it was pityriasis rubra pilaris, but these sections showing the blisters are rather suggestive of pemphigus foliaceus.

Lipodystrophia Progressiva.—C. H. WHITTLE, M.D.

D. C., a married woman, aged 36.

Six years' history of swelling of legs. The legs have become steadily thickened, the natural shape lost and the face and neck at the same time have got thinner and she now has a drawn cadaverous expression. Her face very strikingly resembles the face of another woman with the same condition under my care about six years ago (seen also by Dr. Parkes Weber). A photograph taken some years ago shows the change in this patient.

The legs besides their swollen appearance are cyanotic. The swelling is probably due to deposit of fat. Investigations have included basal metabolic rate, serum calcium and phosphorus, X-rays of the humerus, tibia and fibula: all normal. The suggestion of possible association with parathyroid tumour is not therefore supported in this case.

There were mental disturbances in my first case, chiefly depression. This patient also shows an anxious nervous disposition and has been recently under treatment by a psychiatrist.

No treatment is known to be of any value for the condition.

Dr. F. Parkes Weber: I have seen several examples of this so-called "lipodystrophia progressiva" since I brought forward a case at the Neurological Section of this Society (*Proceedings*, 1913, 6, 71). I would point out that the present patient shows some œdema resulting from chronic hypostatic congestion in addition to the accumulation of fat in the lower extremities. That is likely to happen in many cases, especially when there are slight varicose veins. The question arises whether atypical cases with an enormous accumulation of fat about the pelvis and thighs may be seen without the very striking fat atrophy of the face. The cases which I have seen in boys have not shown any special increase of fat in the lower part of the trunk and thighs.

Dr. E. W. Prosser Thomas: I had a woman patient of about 60 in whom the skin of the lower abdomen, buttocks, thighs, legs, and (to a lesser extent) of the extensor surface of the arms hung in large flabby folds. The face and upper part of the trunk were relatively unaffected. Her skin had apparently always been like this. I do not know whether her condition is due to an accumulation of fat in these areas or to a loosening of the skin and subcutaneous tissue of the "dermatolysis" class. Section merely showed an excess of fat.

Comedones in an Unusual Position.—C. H. WHITTLE, M.D.

W. H., a soldier aged 20.

Nine months' history of small nodules on penis. Much complaint of itching and pain which "hinders his work".

A seborrhœic subject with a scurfy scalp and scars of boils on his neck.

The Pathological Department, Radcliffe Infirmary, reported "inclusion dermoid" on a biopsy taken at Dr. Carleton's request.

This is a soldier I saw a week ago about whom his Medical Officer was worried. The lesions are on the penis. They are in three grades: (1) An exaggeration of the comedones that one does see quite frequently, and which may be said to come within the normal, but in this case one can express sebaceous material from the follicle; (2) yellowish brown follicular papules about 2 mm. in diameter; (3) rather large inflammatory papules on the prepuce.

There is a difference of opinion regarding the histology. A biopsy had been done by the pathologist at Oxford, who stated it was an inclusion dermoid. Clinically, I think the lesions are all follicular, but the section can be interpreted as either an inclusion dermoid or a comedo.—(Section shown by courtesy of Dr. Alice Carleton).

The President: It is a question of whether the contents of the cyst is sebaceous material or horn cells.

Dr. C. H. Whittle: It appears to be causing the man some discomfort, but if it is simply a follicular lesion it should clear up with salicylic acid.

The President: Has the fact that he gets his trousers rather oily while doing mechanics' work on motor vehicles any bearing on the condition?

Dr. C. H. Whittle: In the absence of any other explanation I think that may be the correct one.

Dr. Louis Forman: I think this is an occupational disease. I found the same condition in a soldier who, before he went into the army, had been working on munitions and getting his clothing and skin oily. There were papules with horny plugs over the thighs, abdomen and genitals. What was interesting was the time it took to get him reasonably well.   He was in hospital for three months.

Dr. F. Parkes Weber: This seems to be an instance where there has not been a proper liaison between the clinical pathologist and the clinician.   The pathologist should, if possible, see the cases on which he pronounces.

Case of Pili Torti.—GRACE GRIFFITH, M.B.

Ruth P., aged 3½ years, attended out-patients because of scanty and brittle hair which was constantly breaking off.

On examination the hair was fair with a shimmering glint and looked brush-like, standing off the scalp. Each hair was from 3-8 cm. long, the shorter ones being over the temples and at the back of the scalp, which appeared healthy. The hair felt dry and stiff.

Examining a single hair it looked almost colourless and had sharp bends, some to one side and some to another. No nodes were visible to the naked eye and the break in the hair took place at a bend or twist. The hairs were also flat and ribbon-like. These appearances were verified microscopically, the bends showing as a definite twist through 90° to 180° and the flat straight portions having no visible pigment, so that the structure of the hair showed up very plainly. The eyebrows had a similar tendency.

No other member of the family was known to have a similar condition. Nails were normal. The child had never had any severe illness and the condition had been present since birth.

A similar case was reported by F. F. Hellier in the *British Journal of Dermatology and Syphilis* for June 1940, and he gives a detailed account of previously described cases and of investigations carried out at Leeds to discover the nature of this malformation.

The condition of pili torti has a superficial resemblance to monilethrix but the latter shows nodes and not twists and the hair is round and not ribbon-like, and there is normal pigment in parts. An essential characteristic of pili torti appears to be that the hair is flat and ribbon-like rather than round on transverse section.

This condition of ribbon-like hair was noted by J. M. H. MacLeod in his reference to a case of "knotted hairs" in the *Brit. Journ. Derm.*, 1907, 19, 40, to which he gave the name originally given by Galewsky—Trichonodosis. There is no note on twisting of these flat hairs only knotting but they share the ribbon-like character which is absent in other conditions of imperfect hair.

Clinical Section

President—J. D. ROLLESTON, M.D.

[*November* 12, 1943, *continued*]

MEETING AT ST. MARY ABBOTS HOSPITAL, LONDON

Bilateral Recurrent Spontaneous Pneumothorax.—R. C. BROCK, M.S. (shown by R. LAIRD, Ch.M.).

D. H., female, aged 39.

History.—Bronchopneumonia at age of 14. June 1936 normal pregnancy and labour. February 1939 admitted to hospital with miscarriage at 3 months; uterus curetted and a day or so later became dyspnoeic. X-ray: Spontaneous pneumothorax on left side; this cleared up satisfactorily. Two months later dyspnœa recurred due to right spontaneous pneumothorax which persisted in spite of removal of air.

July 1939 admitted to hospital with right pneumothorax. Thoracoscopy showed almost complete collapse of whole of right lung. No abnormality visible on surface of lung to account for the pneumothorax. Further thoracoscopy performed and iodized talc applied to surface of lung. Air then removed and lung re-expanded. X-ray of chest: No evidence of intrapulmonary disease.

In 1940 a left spontaneous pneumothorax occurred while patient was in Scotland. Readmitted to hospital October 1943. Successful result was obtained after two injections of silver nitrate.

Dr. J. Burnford commented on the ætiological aspect of the case. He noted that the patient had had bronchopneumonia during the influenza pandemic of 1918. In an article (*Proc. Roy. Soc. Med.*, 1919, 12, 49 to 74) at that time he had recorded the pathological changes in the parenchyma of the lungs which he then called influenzal pneumonitis. The changes included friability of the lung tissue and emphysema both microscopic and macroscopic (fig. 1). He emphasized the incidence of acute emphysema as the result of destructive lesions in children suffering from acute bronchopneumonia and he pointed out that cases of chronic pulmonary disease as asthma, emphysema, &c., could be antedated at times to an attack of influenza or bronchopneumonia in infancy.
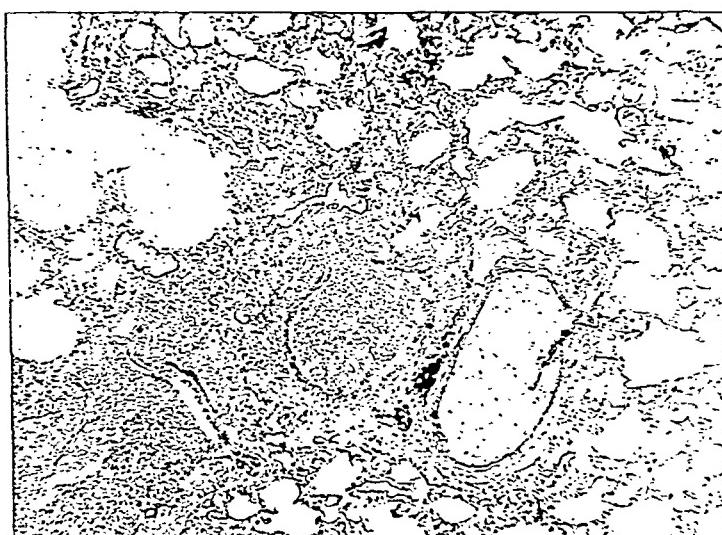
FIG. 1.—Acute emphysema and bronchopneumonia in influenzal pneumonitis. (Section by Dr. Elworthy, Salonika, 1918.)

Fragilitas Ossium.—A. D. WINTON JONES, F.R.C.S.

M. C., female, aged 23.

History.—Nine fractures in all, three prior to the age of 5 years. The others occurred as follows: Fingers at 8 years, right wrist at 12 years, right elbow at 13 years, ring finger at 17 years, ribs at 21 years, sacrum recently. All caused by slight falls. Patient had blue sclerotics.

Family history.—Mother, blue sclerotics, deaf. Brother, blue sclerotics, 3 fractures. Aunt, blue sclerotics, 2 fractures. Three cousins with blue sclerotics, 0, 4 and 2 fractures respectively (*see* fig. 1).

FIG. 1.—B = Blue sclerotics. The figures in brackets indicate the number of fractures.

[*December* 10, 1943]

MEETING AT THE HOSPITAL FOR CONSUMPTION AND DISEASES OF THE CHEST, BROMPTON, LONDON

Bilateral Pleural Effusion.   Eosinophilia and Subcutaneous Nodules: For Diagnosis.— J. L. LIVINGSTONE, F.R.C.P. (shown by NEVILLE SOUTHWELL, M.B., M.R.C.P.).

Female, aged 24. No significant family history. 1935: Five months' illness with cough, wasting, vomiting and dyspnœa. 1937: Started to get asthmatic attacks. April 1941: Joined W.A.A.F. February 1943: Left pleural effusion with 93% of eosinophils. This was air-replaced but continued to accumulate and in March 1943 right pleural effusion developed and she was admitted to Brompton. Pyrexia every three weeks until June when she became afebrile. *Spleen was palpable; no glands. X-ray: Bilateral pleural* effusion. Opacity in left upper zone—some scarring at right apex which gradually disappeared. Fluid was repeatedly aspirated from both pleuræ; it always contained a high percentage of eosinophils. T.B. not found. Slight leucocytosis with up to 27% of eosinophils. No evidence of hydatid disease, intestinal parasites or trichiniasis. Mantoux (P.P.D. 0·00002 mg.) faint positive. September 1943: Transferred to Robertsbridge Sanatorium, slightly improved. October 1943: Swellings on both forearms, pain and numbness in fingers of right hand. Readmitted to Brompton. Small subcutaneous nodules not attached to skin on both forearms. ? peripheral involvement of right median nerve. Biopsy left forearm: Nodule in muscle. Histology: Necrotic areas with many giant cells, eosinophils, plasma cells and fibroblasts.

Dr. A. Elkeles suggested a diagnosis of polyarteritis nodosa. Within the last two years he had observed three cases of polyarteritis nodosa. The occurrence of asthmatic attacks in the history of this disease had been stressed by several authors and this fact had been used as one of the arguments to prove its allergic background. Asthmatic attacks had occurred in his cases. Another characteristic feature of the disease was the great variety and the fleeting character of the lesions. X-ray examination of the chest contributed to the diagnosis. In one of his cases the changes in the lungs were followed up over a period of several months by serial X-rays. The characteristic features were transitory infiltrations in the left upper lobe with interconnecting streaks towards the upper segment of the hilum; these appearances being very similar to tuberculous infiltrations. This stage coincided with marked eosinophilia in the blood. The lesions disappeared without leaving any trace in later X-ray examinations. Transitory infiltrations in the lungs associated with eosinophilia had been described and were known as Loeffler's syndrome. In polyarteritis nodosa the dominant and more permanent lesions could be seen in the distribution of the pulmonary vessels within the hilar regions and extending to the lower lobes above and even below the shadow of the diaphragm. They formed dense streaky shadows and on close inspection tortuosity and dilatation could be seen in the larger branches. The additional fibrosis contributed later to the density of the non-homogeneous shadows which were more intense in the central hilar region and faded gradually towards the periphery. These changes became complicated by bilateral effusions which disappeared and returned to a greater extent in the terminal stages of the disease.

Dr. Eli Davis stated that trichiniasis could be excluded, judging from the 26 cases he had described with Allott (*Lancet*, 1941 (ii), 396).

Mr. A. Dickson Wright said that the diagnosis of this notoriously difficult disease carried with it a very characteristic X-ray picture of the lung fields. Dr. Elkeles had drawn attention to this characteristic infiltration pattern so that by X-raying the only translucent viscera of the body we had the key to still another somatic disease in addition to Boeck's sarcoidosis and erythema nodosum.

Intrathoracic Tumour: For Diagnosis.—MAURICE DAVIDSON, F.R.C.P., and R. C. BROCK, F.R.C.S.

Female, aged 24, in the W.R.N.S., who had always enjoyed good health, complained suddenly of stabbing pains in the left side of the chest. The M.O. to whom she reported sick found a slight pleural rub in the left axilla and took her into the sick bay ‖for observation. A day or two later she felt better and the signs of pleurisy had cleared up. On X-ray examination at Brompton, however, a large opacity was seen in the upper third of the chest on the left side: the lower edge of the opacity was well defined and the appearances suggested the presence of a benign tumour, though the possibility of an encysted effusion was also considered. The X-ray pictures bore a close resemblance to those of other cases exhibited, in which neurofibromata had been discovered on surgical exploration and successfully removed.

In this case it was decided to put in an exploring needle. When this was done about 2 oz. of blood-stained fluid were removed from what felt at the time like a semi-solid, partly cystic, tumour. A few days later the patient became very dyspnœic and developed signs of a large pleural effusion on the left side. Aspiration was performed and over 30 oz. of fluid, which looked almost like pure blood, were removed. In view of this phenomenon and also of the appearance within a week or so of her admission of a large and rather hard lymph node beneath the left sternomastoid, it was concluded that the original tumour in the chest must be a rapidly growing and malignant neoplasm of mesoblastic origin. The patient has been transferred to the Royal Cancer Hospital where deep X-ray therapy has been started in the hope that the growth may prove to be radio-sensitive. The patient's general condition, however, has deteriorated appreciably since she first went sick, and the outlook at the moment appears to be very grave.

POSTSCRIPT (February 8, 1944).—After several weeks of radiotherapy the secondary lymph node has disappeared and the primary tumour has diminished appreciably in size, Cough and dyspnœa are now absent: the patient's general condition is much better.

Bilateral Spontaneous Pneumothorax in an Asthmatic.—MAURICE DAVIDSON, F.R.C.P., and R. C. BROCK, F.R.C.S. (shown by JEAN C. WILSON, M.B.).

Female, aged 16. Asthma since age of 3. April 1943: Left spontaneous pneumothorax with recurrence in July 1943, followed by collapse of right lung. Admitted to Brompton August 1943. X-ray: Bilateral spontaneous pneumothorax. E.S.R. 1/200. Silver nitrate introduced into both pleural cavities to promote adhesions.

Pneumonectomy for Bronchiectasis.—W. E. LLOYD, F.R.C.P., and C. PRICE THOMAS, F.R.C.S. (shown by A. F. FOSTER-CARTER, D.M.).

Female, aged 6. Lobar pneumonia aged 2, followed by persistent cough and profuse sputum. Several attacks of acute pneumonia during past four years. April 1943: Admitted to Brompton. Febrile to 100°, persistent cough. X-ray: Fibrosis, pleural thickening and bronchial dilatation throughout left lung. Heart displaced to left. Right lung: Compensatory emphysema. 23.9.43: Left dissection pneumonectomy. Lung densely adherent. Patient made an uninterrupted recovery without infection of the pleural space, and is now symptom-free.

Solitary Cyst of Lung. Lobectomy.—CLIFFORD HOYLE, F.R.C.P., and C. PRICE THOMAS, F.R.C.S.

Female, aged 19 months. Frequent colds since age of 5 months. July 1942: Cough with sputum and vomiting. August 1942: Admitted to Brompton. Signs of left pneumothorax. Heart and trachea displaced to right. X-ray: Large cyst occupying left chest. 29.10.42: Left upper lobectomy. Large, thin-walled cyst occupying almost the whole left upper lobe. Lower lobe completely collapsed. Upper lobe and cyst removed with tourniquet. Lower lobe showed signs of re-expansion at the end of operation.

Fragilitas Ossium.—A. D. WINTON JONES, F.R.C.S.

M. C., female, aged 23.

History.—Nine fractures in all, three prior to the age of 5 years. The others occurred as follows: Fingers at 8 years, right wrist at 12 years, right elbow at 13 years, ring finger at 17 years, ribs at 21 years, sacrum recently. All caused by slight falls. Patient had blue sclerotics.

Family history.—Mother, blue sclerotics, deaf. Brother, blue sclerotics, 3 fractures. Aunt, blue sclerotics, 2 fractures. Three cousins with blue sclerotics, 0, 4 and 2 fractures respectively (*see* fig. 1).

FIG. 1.—B = Blue sclerotics. The figures in brackets indicate the number of fractures.

[*December* 10, 1943]

MEETING AT THE HOSPITAL FOR CONSUMPTION AND DISEASES OF THE CHEST, BROMPTON, LONDON

Bilateral Pleural Effusion.   Eosinophilia and Subcutaneous Nodules: For Diagnosis.— J. L. LIVINGSTONE, F.R.C.P. (shown by NEVILLE SOUTHWELL, M.B., M.R.C.P.).

Female, aged 24. No significant family history. 1935: Five months' illness with cough, wasting, vomiting and dyspnœa. 1937: Started to get asthmatic attacks. April 1941: Joined W.A.A.F. February 1943: Left pleural effusion with 93% of eosinophils. This was air-replaced but continued to accumulate and in March 1943 right pleural effusion developed and she was admitted to Brompton. Pyrexia every three weeks until June when she became afebrile. Spleen was palpable; no glands. X-ray: Bilateral pleural effusion. Opacity in left upper zone—some scarring at right apex which gradually disappeared. Fluid was repeatedly aspirated from both pleuræ; it always contained a high percentage of eosinophils. T.B. not found. Slight leucocytosis with up to 27% of eosinophils. No evidence of hydatid disease, intestinal parasites or trichiniasis. Mantoux (P.P.D. 0·00002 mg.) faint positive. September 1943: Transferred to Robertsbridge Sanatorium, slightly improved. October 1943: Swellings on both forearms, pain and numbness in fingers of right hand. Readmitted to Brompton. Small subcutaneous nodules not attached to skin on both forearms. ? peripheral involvement of right median nerve. Biopsy left forearm: Nodule in muscle. Histology: Necrotic areas with many giant cells, eosinophils, plasma cells and fibroblasts.

Dr. A. Elkeles suggested a diagnosis of polyarteritis nodosa. Within the last two years he had observed three cases of polyarteritis nodosa. The occurrence of asthmatic attacks in the history of this disease had been stressed by several authors and this fact had been used as one of the arguments to prove its allergic background. Asthmatic attacks had occurred in his cases. Another characteristic feature of the disease was the great variety and the fleeting character of the lesions. X-ray examination of the chest contributed to the diagnosis. In one of his cases the changes in the lungs were followed up over a period of several months by serial X-rays. The characteristic features were transitory infiltrations in the left upper lobe with interconnecting streaks towards the upper segment of the hilum; these appearances being very similar to tuberculous infiltrations. This stage coincided with marked eosinophilia in the blood. The lesions disappeared without leaving any trace in later X-ray examinations. Transitory infiltrations in the lungs associated with eosinophilia had been described and were known as Loeffler's syndrome. In polyarteritis nodosa the dominant and more permanent lesions could be seen in the distribution of the pulmonary vessels within the hilar regions and extending to the lower lobes above and even below the shadow of the diaphragm. They formed dense streaky shadows and on close inspection tortuosity and dilatation could be seen in the larger branches. The additional fibrosis contributed later to the density of the non-homogeneous shadows which were more intense in the central hilar region and faded gradually towards the periphery. These changes became complicated by bilateral effusions which disappeared and returned to a greater extent in the terminal stages of the disease.

more on right. Axillæ: One soft gland on left. Arms: No clubbing of fingers; hands blue and cold. Chest—Heart: Apex beat in 5th space ½ in. outside nipple line. Sounds normal. B.P. 130/20. Percussion note impaired to right of sternum. Vocal fremitus equal. Breath sounds faint all over. Some crepitations and sibili low down in front and behind. Both mammary glands were large, resembling those of many girls of his age. Both testicles atrophied. X-ray showed a large bilateral mass mainly in the anterior mediastinum. During the next three weeks pressure signs increased rapidly. The neck became full and enlarged veins appeared on the upper part of the chest. An aspiration biopsy was attempted but only blood was obtained.

11.5.43: Transferred to St. Bartholomew's Hospital for deep X-ray therapy. A month later the tumour had practically disappeared, and all chest signs had gone. No venous distension in neck, though the veins on the upper chest were still obvious.

Now, six months later, he remains well. X-ray shows no recurrence. Mammary enlargement still present, but definitely less and veins of neck and chest normal.

POSTSCRIPT (February 10, 1944).—No signs of recurrence of tumour.

Hæmangio-Endothelioma of Chest Wall.—J. E. H. ROBERTS, O.B.E., F.R.C.S.

A. H. W., male, aged 69. About the beginning of June 1943 the patient stated a lump suddenly came up on the left upper chest. No symptoms. 21.7.43: Admitted to Hill End Hospital Thoracic Unit.

On examination.—There is a visible and palpable swelling below the left clavicle about 4½ in. in diameter and extending from its lower border to the 3rd rib and from the edge of the sternum almost to the anterior axillary line. The swelling is not entirely homogeneous, the medial portion being more prominent and very elastic, while the upper and the lateral parts are flatter and fairly firm in consistency. The skin over the tumour is not hot or red and is freely mobile. There are some dilated veins over the tumour, the blood running medially. The swelling is fixed to the deeper structures, and tensing of the pectoralis major only anchors it a little more firmly. It is not tender. It is dull to percussion, it does not pulsate nor has it an impulse on coughing. No bruits are heard. X-ray: A large spherical opacity in the left upper chest. The anterior end of the 2nd rib is missing and the 3rd rib is displaced downwards. The opacity extends backwards to the level of the vertebræ.

26.7.43: Attempted biopsy. Small transverse incision made over swelling, the pectoralis major was split and a thin-walled cystic swelling exposed. On aspiration thin brown fluid was obtained. A small incision was made and the fluid was evacuated. Profuse hæmorrhage then followed, so the cavity was tightly packed with gauze. The packing was changed every few days until 19.8.43, when a biopsy was taken from the anterior and posterior walls of the cavity, and the packs replaced by a tube.

Histological report (Prof. Hadfield): Anterior chest wall neoplasm. The large brownish masses are composed of autolysing fibrin. The small white opaque masses are composed of tumour tissue. In some places this is highly cellular. The cells have the general characters of vasoformative endothelium. They tend by vacuolation to produce endothelial lined spaces after the manner of angioblasts. As the result of this process the tumour tissue contains cystic spaces of all sizes, the largest being filled by colloid material, the smallest by blood. These characters are those of hæmangio-endothelioma. It is probable that the tumour has existed for some time but the striking cellularity of some parts of it suggests that there has been rapid growth recently and that the tumour has malignant potentialities.

In view of the patient's age and the extensive removal of the chest wall which would be necessary, it was decided to treat by therapeutic X-rays. A full course of deep X-rays has been given at St. Bartholomew's Hospital.

POSTSCRIPT (February 10, 1944).—Patient remains well in himself. The tumour is still present but has not grown larger.

Assmann's Focus.—CLIFFORD HOYLE, F.R.C.P. (shown by NEVILLE SOUTHWELL, M.B., M.R.C.P.).

Female, aged 27. Hospital nurse. No significant family history. Opacity discovered on routine examination January 1942. August 1943: Slightly larger. No symptoms at any time. October 1943: Admitted to Brompton. X-ray: Rounded opacity in apex of left lung suggesting neurofibroma. After diagnostic A.P. the shadow appeared to be intrapulmonary. ? Assmann's focus.

AUTHOR'S NOTE (30.12.43): The final diagnosis of this case was intrapulmonary consolidation, i.e. an Assmann's focus, and, after thoracoscopy and adhesion section, the condition subsided. The patient is symptom-free and is going to a sanatorium.

Persistent Spontaneous Pneumothorax.—GEOFFREY MARSHALL, F.R.C.P., and R. C. BROCK, F.R.C.S. (shown by JEAN C. WILSON, M.B.).

Male, aged 40, July 1943, while in Army, sudden pain in right chest and dyspnœa: Right pneumothorax diagnosed in military hospital and 500 c.c. air removed. Ten weeks later another 400 c.c. removed. September 1943: Admitted to Brompton. Some dyspnœa and palpitation. X-ray: Complete right pneumothorax. Aspiration of 1,000 c.c. air produced only temporary improvement. 19.10.43: Thoracoscopy (Mr. Brock): Emphysematous bulla on upper lobe which was held up by two adhesions, air bubbled out through a small fissure at the base of one of these. This area was painted with 10% silver nitrate. Lung completely re-expanded following second injection (m VII) of 10% silver nitrate.

Mr. Ivor Lewis inquired if in this case the adhesions had been divided. Gullbring of Stockholm had shown that some of these cases were due to an adhesion holding out a ruptured bulla. Since some of these cases at Gullbring's hospital, the speaker had himself seen one or two such cases of persistent tension pneumothorax, showing a ruptured bulla at the base of an adhesion, both adhesions and bulla being beautifully shown in the X-ray in one case. What happened in such a case was that, as soon as the adhesion was divided, the half-lifted fragment of visceral pleura was allowed to fall as a lid over the tear, abolishing the valvular effect, and so promoting the rapid healing of the tear. A case of his had rapidly expanded after thoracoscopy and severance of the string adhesion, without any further treatment.

Constrictive Pericarditis with Calcification: Partial Pericardectomy.—W. E. LLOYD, F.R.C.P., and C. PRICE THOMAS, F.R.C.S.

Male, aged 39. No history of rheumatism or serious illness. September 1933: Noticed swelling of face. Recurred in January 1934 with dyspnœa; treated in hospital for seven weeks. Well and working until January 1940 when face, neck, abdomen and ankles began to swell; dyspnœa on slight exertion, completely incapacitated. February 1940: Admitted to Brompton. Congestion of face with prominent veins. Apex beat not clearly palpable. Heart sounds muffled; no bruits. Pulses equal and regular. B.P. 112/86. Dilated veins over abdomen filling from above. Liver enlarged three fingers below costal margin. Moderate ascites. Sacral œdema. Ankles œdematous. Circulation times, arm-lung: 11·5 sec. Arm-tongue: 17 sec. Venous pressure: 22 cm. of water. X-ray: Pericardial calcification; small left basal effusion. Improved with rest and diuretics. April 1940: Partial pericardectomy (Mr. Price Thomas). About 3 in. by 3 in. of anterior surface of pericardium removed. Uneventful recovery. Symptoms relieved. Has been back at work as a carpenter since September 1940.

Mediastinal Teratoma.—J. E. H. ROBERTS, O.B.E., F.R.C.S.

J. W., female, aged 20. No symptoms apart from very slight cough and recent slight breathlessness on going upstairs. When examined under mass radiography scheme was found to have a mediastinal tumour and was admitted to Brompton under Dr. F. H. Young. No abnormal physical signs on examination. X-rays: Large mass in anterior mediastinum, with shadows suggesting bone or teeth. 22.10.43: Left thoracotomy: After incising the pleura which covered it, the tumour was easily shelled out intact; the vessels entering it at its upper pole were ligated. During this procedure the phrenic nerve was probably pinched as the diaphragm became immobile. The chest was closed without drainage after reinflating the lung. 23.10.43: 12 oz. heavily blood-stained fluid was aspirated from the pleura. A portable X-ray showed collapse of the lung. During the next few days fluid was aspirated three more times. The lung re-expanded and she returned home on the twenty-first day after operation.

Examination of tumour: A partly cystic mass containing sebaceous material but no hairs in the main space. Smaller cysts did contain hairs. There was a mass of apparently true bone and cartilage.

Mediastinal Tumour (? Thymoma) with Gynæcomastia.—J. E. H. ROBERTS, O.B.E., F.R.C.S.

H. S., male, aged 16. March 1943: Sudden onset of pain in right chest, in axilla and in front, stabbing in character. Pain disappeared in two days. X-ray showed a large shadow. 16.4.43: Admitted to Hill End Hospital Thoracic Unit. No pain, slight cough. No hæmoptysis. In last three weeks has been breathless on exertion. Has lost 10 lb. in about three months.

On examination.—Neck: No glands palpable; soft swelling, slightly to right of mid-line in suprasternal notch, smooth, not tender. Bilateral distension of external jugular veins,

Section of Ophthalmology

President—F. A. JULER, F.R.C.S.

[*November* 12, 1943]

Intra-ocular Foreign Body.—J. W. E. CORY, M.D.

A Post Office engineer, aged 37, was seen on October 12, with a history of having got something in his right eye three days previously.

A large metallic foreign body was seen lying in, or just posterior to, the posterior capsule of the lens. There is a small entrance wound at 2 o'c., 2 mm. from the limbus, but no visible injury to the iris—nor was there any such evidence when first seen.

The vision is R. 6/60 (previous to accident 6/36 improving to 6/9) and L. 6/6. The fragment, which is part of a brass cotter pin, shows indistinctly in the X-ray and the body is non-magnetic.

There seems to be very little reaction after five weeks and I propose to leave him alone unless he develops a cataract.

POSTSCRIPT (18.2.44).—Appearances remain unchanged.—J. W. E. C.

Flocculi.—R. A. D. CRAWFORD, M.B., D.O.M.S. (introduced by Major E. F. KING, R.A.M.C.).

This patient, a soldier aged 25, had no trouble with his vision and no one ever noticed anything peculiar about his eyes until he complained of blurring of the left eye in strong sunlight. After he had been seen he was sent home for diagnosis. He has flocculi of both irides, larger in the left eye than in the right, and that in the left eye has formed an anterior attachment to the back of the cornea. I have not found any reference to this latter condition in the literature and nobody I have asked has remembered ever seeing it. The condition apparently results from a failure of closing and cystic dilatations of the marginal sinus (*see* figure).
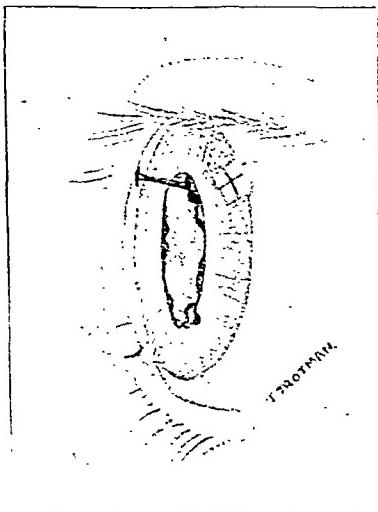
Flocculus with anterior attachment to the cornea.

Tuberculoma of Lung. Removed by Lobectomy.—R. C. BROCK, F.R.C.S.

Female, aged 52. No significant family history. July 1943: One pint hæmoptysis. August 1943: Repeated hæmoptyses and occasional pain in right chest. X-ray: Localized opacity in right lower zone. Bronchogram: Bronchus leading to opacity does not fill. No fever, no sputum. Bronchoscopy: No abnormality visible in bronchial tree. 2.11.43: Right lower lobectomy. Lesion found on lateral surface of lower lobe. Depressed, hard and nodular having appearance of a scirrhous carcinoma. Lower lobe removed by dissection. Bronchus closed with intercostal muscle graft. Post-operative progress satisfactory. Section of "tumour" showed tuberculous tissue.

Pulmonary Tuberculosis Treated by Pneumoperitoneum.—F. H. YOUNG, O.B.E., F.R.C.P.

Male, aged 37. No significant family history. Pleurisy November 1940, febrile attack December 1941, Cheam Sanatorium February 1942, sputum positive. Admitted to Brompton, September 1943. X-ray: Right basal infiltration with some collapse. Afebrile; B.S.R. 14/200, sputum one oz. T.B. positive. 27.9.43: Right A.P. induced. Unsatisfactory collapse. 11.11.43: Right phrenic crush. 23.11.43: Induction of pneumoperitoneum.

Pulmonary Tuberculosis Treated by Pneumoperitoneum.—F. H. YOUNG, O.B.E., F.R.C.P.

Male, aged 30. No significant family history. Winter cough four years. Worse last winter, with lassitude and pain in right chest. Pulmonary tuberculosis diagnosed September 1943. Sputum T.B. positive. Admitted Frimley Sanatorium. X-ray: Extensive infiltration right base with two large cavities. 4.10.43: Right A.P. induced. Cavities unaffected. November 1943: Admitted to Brompton for adhesion section. Thoracoscopy (Mr. Price Thomas): Lower lobe widely adherent in paravertebral gutter. 25.11.43: Pneumoperitoneum induced. 30.11.43: Right phrenic crush.

the Council's own clinics), there were only 9 cases of ophthalmia neonatorum amongst them (or 0·5 per 1,000), but amongst the 1,625 emergency cases which had had no ante-natal care, or had received it from other services, 8 cases had arisen or 5·0 per 1,000. None of these 17 patients had a known history of gonorrhœa. A few had had vaginal discharge but bacteriological examination had proved negative. 13 of these 17 mothers were positive to the gonococcus after delivery, 2 were 'suspicious" and 2 refused to co-operate.

The prophylaxis used for infants in the London County Council wards was very much on the lines Professor Sorsby had decribed and the variety of drug employed seemed to matter little. The figures showed that ante-natal care seemed the main preventive factor, but a certain number of cases did slip through in spite of very careful ante-natal work.

Professor Chassar Moir said that a slight inflammation of the eyes was very common in the first week of life. Cases of "sticky eye" were often not notified, and discrepancies in statistics could be largely explained by this fact.

As prophylaxis against gonococcal ophthalmia, silver nitrate has stood the test of time, but it was also true that silver nitrate solution was irritating and frequently pro-duced a chemical inflammation of its own. In all cases of inflammation it was his practice to wipe the conjunctiva with a minute swab, and to examine the pus for himself: very often no organisms were present, or, at the most, a few were found after prolonged search. He imagined that such cases were usually examples of chemical irritation, and his belief was strengthened by the fact that after the use of 2% instead of the usual 1% solution, cases of inflammation were much commoner and more severe. Silver nitrate lotions were used in other branches of surgery—but only with discretion. The genito-urinary surgeons, for example, never used the solution in greater strength than 1:500 for a bladder washout. Yet, a solution five times as strong as this was routinely used in the eyes of babies at birth: it was not surprising that severe reactions sometimes occurred.

With these facts in mind he wished to protest against the all too common practice of treating "sticky eyes" by putting in more and more silver nitrate. The possibility of serious harm resulting from the reckless repeated use of silver nitrate—the other name of which was lunar caustic—should be realized. Better methods of treatment were now available.

Mr. Frederick Ridley said that his experience had also been that the use of silver nitrate did undoubtedly lead to a large incidence of "sticky eyes." The treatment of such eyes by silver nitrate drops was definitely harmful. He believed it was dangerous to use even 1% silver nitrate upon a baby's cornea which was already ulcerating and he thought it should be barred. It was a pleasant substance in some respects, but it was very unpleasant when it ceased to be just 1% silver nitrate. The acidity of a 1% silver nitrate solution kept in a tightly-stoppered bottle had reached the figure of pH2. They would not willingly put acid of that concentration into babies' eyes, yet it was done by midwives who kept these bottles in their kit. The concentration also continually increased by evaporation and he had seen silver nitrate crystals formed in a dropper bottle: such drops were capable of blinding a baby. Much of this could be avoided by the use of wax capsules such as Professor Sorsby had mentioned, and which their American col-leagues were using successfully, but in its ordinary form (out of a bottle insecurely stoppered, probably months old and exposed to light), and as treatment by repeated instil-lation, silver nitrate was harmful.

Argyrol was a safe and even more effective prophylactic than silver nitrate, it did not change spontaneously on keeping, even if it became concentrated by evaporation it did not become harmful, it was not easily confused with any other solution such as nitric acid in the midwife's bag, and moreover it was the appropriate drug to use by repeated instillation in the initial stages of an eye infection in a baby, until expert advice could be obtained. He would strongly advocate that argyrol should be used and that silver nitrate should be discontinued as a routine prophylactic.

Squadron Leader L. G. Scoular said that in one of Professor Sorsby's tables he demon-strated that argyrol in strength of 5 to 20% was better than 2% of silver nitrate. Why should they go to the trouble of making up the silver nitrate solution when argyrol, which was a stable preparation, could be used on every child in whom there was a possibility of this infection developing?

Professor Sorsby, in reply, said it was futile to rely upon one solitary measure for the elimination of ophthalmia neonatorum. In the whole range of public health there was no procedure which would rely on one drop of an antiseptic to prevent the development of infection in people who had been exposed to it. Ante-natal care was extraordinarily important as the figures had shown.

In very many institutions silver nitrate was used as a standard method, it had been used in millions of births so that it could not be so desperately dangerous as some people believed. That did not mean, however, that there were no better drugs. The figures obtained from lying-in hospitals possibly showed argyrol to be superior to silver nitrate but the series was too small from which to judge.

Rupture of Retinal Cyst Causing Retinal Detachment.—Major C. Dee Shapland, R.A.M.C.

J. S., aged 28, was sent to the hospital on September 20, 1943, on account of failing vision in the right eye noticed for the previous six weeks. The acuity of the right eye was recorded as 6/6 unaided on his examination by a civilian medical board on April 20, 1940, and he was placed in Grade 1, being subsequently re-examined on April 16, 1940, and placed in Army Category A1. He was re-examined medically on June 4, 1942,

The President said that he had never seen an attachment to the cornea of this kind. The common "grape seed bodies" protruded into the pupil, but he had not seen them hanging in the anterior chamber.

Mr. Affleck Greeves did not see why one should use the term "anterior synechia", thus assuming an attachment to the cornea. It seemed to him likely that the mass was not actually attached to, but merely in contact with, the posterior corneal surface against which it was flattened on account of its bulk.

Epibulbar Dermoid with Rupture of Cyst Contents into Anterior Chamber.—VICTOR PURVIS, M.B.

Child brought a year ago at the age of 1 year and 4 months to Moorfields with a history of a swelling on the right eye since birth that had recently and suddenly increased in size.

On examination it had all the appearances of an epibulbar dermoid, but there was an amount of white flocculent material in close proximity to it in the anterior chamber. It was considered that this material was the contents of a ruptured dermoid cyst. During the next few months the eye became irritable from time to time and the flocculent material absorbed, drawing down the pupil in the process.

Two months ago another mass of material suddenly appeared in the anterior chamber near to the cyst as if the latter had ruptured once more. It is proposed to wash out the anterior chamber to. ascertain the nature of the material and enable a correct diagnosis to be made. If the tumour is a dermoid it is a unique one because they are rarely cystic at this site and are not known to rupture into the anterior chamber in the way described. On the other hand it may be an implantation cyst in spite of the fact that there is no history of injury.

The Incidence and Treatment of Ophthalmia Neonatorum.—Professor ARNOLD SORSBY, F.R.C.S. (*Abstract*).

Incidence.—Ophthalmia neonatorum has been a notifiable disease in England and Wales since 1914 and has shown some decline in incidence. There is, however, considerable variation in the rate of notification in different parts of the country, pointing to different conceptions as to what constitutes notifiable ophthalmia neonatorum. Replies to a questionnaire sent out to lying-in-centres indicate a rate of gonococcal ophthalmia of 0·8 per 1,000 births. On this basis there are annually about 500 cases of this type of ophthalmia neonatorum and a total of about 2,000 cases of all types throughout the country.

The annual returns of the Ministry of Health indicate a steady decline in the incidence of impaired vision and blindness from ophthalmia neonatorum. This is borne out by returns from L.C.C. blind schools, but that blindness from ophthalmia neonatorum is still a problem is also shown by these returns and by the applications for admission to Sunshine Homes for blind babies. The extent of the problem is different in different parts of the country. It does not appear that the incidence of blindness from ophthalmia neonatorum has declined as markedly as that for other infectious diseases.

Prophylaxis.—Antenatal care is of prime importance as is shown by excellent results in eliminating ophthalmia neonatorum at such centres as Sheffield Street (L.C.C.) Hospital for mothers suffering from venereal disease. Prophylactic drops instilled into the eyes of babies at birth are no absolute safeguard against gonococcal ophthalmia, as the occurrence of 98 cases in 119,075 births given in the returns of the questionnaire show. On the basis of these returns the incidence of gonococcal ophthalmia is 0·9 per 1,000 births when silver nitrate is used as a prophylactic and 0·7 per 1,000 with other preparations (generally argyrol).

Treatment.—The immense advance marked by the sulphonamides in the treatment of ophthalmia neonatorum of all types is shown by the fact that in 500 cases treated at White Oak Hospital during January 1940 to October 1943 no less than 72·2% were cured within eight days (against 15·2% of cases treated by the classical method).

Dr. Letitia Fairfield said with regard to the question of notification, that London was the pioneer in collecting cases of ophthalmia neonatorum into a specialized hospital (St. Margaret's now evacuated to White Oak) and under the care of Mr. Cardell. The London notification rate was only about 9 per 1,000 as against the 60 per 1,000 of Birmingham. but the results were very similar.

In 1937 there were 19,222 live and 722 stillbirths in the maternity units of London County Council hospitals and of these 17 developed gonococcal ophthalmia and were admitted to St. Margaret's ophthalmia unit. When the case records were examined it was found that although 17,936 of the births (live and still) in the Council's hospitals in that year were "booked" cases (i.e. had had whole or part of their ante-natal care in

the Council's own clinics), there were only 9 cases of ophthalmia neonatorum amongst them (or 0·5 per 1,000), but amongst the 1,625 emergency cases which had had no ante-natal care, or had received it from other services, 8 cases had arisen or 5·0 per 1,000. None of these 17 patients had a known history of gonorrhœa. A few had had vaginal discharge but bacteriological examination had proved negative. 13 of these 17 mothers were positive to the gonococcus after delivery, 2 were 'suspicious" and 2 refused to co-operate.

The prophylaxis used for infants in the London County Council wards was very much on the lines Professor Sorsby had decribed and the variety of drug employed seemed to matter little. The figures showed that ante-natal care seemed the main preventive factor, but a certain number of cases did slip through in spite of very careful ante-natal work.

Professor Chassar Moir said that a slight inflammation of the eyes was very common in the first week of life. Cases of "sticky eye" were often not notified, and discrepancies in statistics could be largely explained by this fact.

As prophylaxis against gonococcal ophthalmia, silver nitrate has stood the test of time, but it was also true that silver nitrate solution was irritating and frequently pro-duced a chemical inflammation of its own. In all cases of inflammation it was his practice to wipe the conjunctiva with a minute swab, and to examine the pus for himself: very often no organisms were present, or, at the most, a few were found after prolonged search. He imagined that such cases were usually examples of chemical irritation, and his belief was strengthened by the fact that after the use of 2% instead of the usual 1% solution, cases of inflammation were much commoner and more severe. Silver nitrate lotions were used in other branches of surgery—but only with discretion. The genito-urinary surgeons, for example, never used the solution in greater strength than 1:500 for a bladder washout. Yet, a solution five times as strong as this was routinely used in the eyes of babies at birth; it was not surprising that severe reactions sometimes occurred.

With these facts in mind he wished to protest against the all too common practice of treating "sticky eyes" by putting in more and more silver nitrate. The possibility of serious harm resulting from the reckless repeated use of silver nitrate—the other name of which was lunar caustic—should be realized. Better methods of treatment were now available.

Mr. Frederick Ridley said that his experience had also been that the use of silver nitrate did undoubtedly lead to a large incidence of "sticky eyes." The treatment of such eyes by silver nitrate drops was definitely harmful. He believed it was dangerous to use even 1% silver nitrate upon a baby's cornea which was already ulcerating and he thought it should be barred. It was a pleasant substance in some respects, but it was very unpleasant when it ceased to be just 1% silver nitrate. The acidity of a 1% silver nitrate solution kept in a tightly-stoppered bottle had reached the figure of pH2. They would not willingly put acid of that concentration into babies' eyes, yet it was done by midwives who kept these bottles in their kit. The concentration also continually increased by evaporation and he had seen silver nitrate crystals formed in a dropper bottle: such drops were capable of blinding a baby. Much of this could be avoided by the use of wax capsules such as Professor Sorsby had mentioned, and which their American col-leagues were using successfully, but in its ordinary form (out of a bottle insecurely stoppered, probably months old and exposed to light), and as treatment by repeated instil-lation, silver nitrate was harmful.

Argyrol was a safe and even more effective prophylactic than silver nitrate, it did not change spontaneously on keeping, even if it became concentrated by evaporation it did not become harmful, it was not easily confused with any other solution such as nitric acid in the midwife's bag, and moreover it was the appropriate drug to use by repeated instillation in the initial stages of an eye infection in a baby, until expert advice could be obtained. He would strongly advocate that argyrol should be used and that silver nitrate should be discontinued as a routine prophylactic.

Squadron Leader L. G. Scoular said that in one of Professor Sorsby's tables he demon-strated that argyrol in strength of 5 to 20% was better than 2% of silver nitrate. Why should they go to the trouble of making up the silver nitrate solution when argyrol, was a stable preparation, could be used on every child in whom there was a possibility of this infection developing?

Professor Sorsby, in reply, said it was futile to rely upon one solitary measure for the elimination of ophthalmia neonatorum. In the whole range of public health there was no procedure which would rely on one drop of an antiseptic to prevent the development of infection in people who had been exposed to it. Ante-natal care was extraordinarily important as the figures had shown.

In very many institutions silver nitrate was used as a standard method, it had been used in millions of births so that it could not be so desperately dangerous as some people believed. That did not mean, however, that there were no better drugs. The figures obtained from lying-in hospitals possibly showed argyrol to be superior to silver nitrate but the series was too small from which to judge.

Rupture of Retinal Cyst Causing Retinal Detachment.—Major C. DEE SHAPLAND, R.A.M.C.

J. S., aged 28, was sent to the hospital on September 20, 1943, on account of failing vision in the right eye noticed for the previous six weeks. The acuity of the right eye was recorded as 6/6 unaided on his examination by a civilian medical board on April 20, 1940, and he was placed in Grade 1, being subsequently re-examined on April 16, 1940, and placed in Army Category A1. He was re-examined medically on June 4, 1942,

and November 13, 1942, and no change made in his category. On August 2, 1943, the day before he first noticed the right vision to be misty, he had felt a sudden sharp. shooting pain lasting some two to three minutes in the region of the right temple "just where the veins are" and felt giddy and faint. He was marching out of camp at the time in full equipment with steel helmet.

On examination on September 20, 1943, the right eye was white, there were no keratitic precipitates, the pupil was active and tension normal. A flat detachment of the retina was present temporally extending from 6.30 to 11 o'c., and from 7 to 9 o'c. there was a prominent thin-walled retinal cyst, with ragged dialysis from 7.30 to 9 o'c. The interesting feature exhibited in this case was a linear band of retino-choroidal pigmentary disturbance delimiting the periphery of the cyst above and below. This disturbance was such as is usually seen at the high water mark of static retinal detachments of long standing. Therefore the cyst was old.

It had evidently ruptured at its peripheral attachment at or just behind the ora serrata and the delimiting band of choroido-retinal adhesions had given way over the nasal (inner) part of the cyst so occasioning a spreading detachment of the retina over the temporal half of the fundus. The macula was involved in the detachment and central vision reduced to 3/60, not improved. The visual field was materially contracted nasally.

Operation was performed on September 24, 1943, under surface 4% cocaine and sub-Tenon's capsule 4% novocain anæsthesia. The external rectus was detached and a barrage of surface diathermy applications at 70 ma. placed round the periphery of the scleral surface marking of the cyst. One needle puncture at 40 ma. was made over the centre of the cyst and another at 6.30 o'c. 12 mm. from the limbus. Patient was kept in bed in the Fowler position with both eyes padded for a fortnight and was allowed up for an hour on the fifteenth day. The retinal detachment went back and the cyst was smaller and outlined by a zone of diathermy reactions. The contraction of the latter had appeared to pull down the wall of the cyst and so cause the whole to shrink. The dialysis, on the other hand, was still clearly visible and open. The retina was in place. central vision 6/24 partly. and the field full except for a defect on the nasal side corresponding to the cyst and diathermy reactions.

The interest of the case is that a retinal dialysis, as I had long suspected, can definitely be produced by the rupture of a cyst, that little or no trauma—direct or indirect—can occasion its rupture, that in this case the periphery of the cyst tended to be sealed off by a zone of spontaneously formed retino-choroidal adhesions and that a portion of these gave way on the formation of the dialysis and so occasioned a spreading detachment of the retina.

Mr. C. B. Goulden said that the connexion between retinal cyst and disinsertion had long been suspected and some suggestive findings by Weve of Utrecht gave support to this possibility as he had found that the retroretinal fluid removed in cases of disinsertion had similar enzymes to those found in the fluid from a retinal cyst. There was no doubt that cases of retinal cyst should be operated upon before they gave rise to disinsertion as they were much more easily managed than when disinsertion and subsequent detachment of the retina had occurred.

Dr. T. H. Whittington said that he recalled three cases of retinal cysts. One was a man who came for a detached retina due to a disinsertion and in making the routine examination of his eyes an unruptured peripheral cyst was found at exactly the corresponding spot in the other eye. The second case was a nurse who had a disinsertion which looked just like a ruptured cyst and it seemed to be so as there was an unruptured cyst of similar appearance close by. Both cases were successfully dealt with. The third case was now under treatment.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*November 26, 1943*]

DISCUSSION ON INFECTIVE HEPATITIS: RECENT FIELD INVESTIGATIONS

Infective Hepatitis in Leicestershire: A Survey of 1,062 Cases

Dr. Arthur A. Lisney (*Deputy County Medical Officer and Deputy School Medical Officer, Leicestershire County Council*): The first recorded epidemic of infective hepatitis in Leicestershire was an outbreak in the Castle Donington area described by Montford (1934). As far as I can ascertain no references to individual cases or outbreaks of this disease were published previously, either in the annual reports of the county medical officer of health, or elsewhere, though no doubt infective hepatitis has occurred for many years in the county both in endemic and epidemic form.

According to Hirsch (1886) the first epidemic of jaundice to be recorded in this country was a series of cases exclusively among children that occurred from September to November 1852 in Birmingham, not so far distant from Leicestershire. Outbreaks occurred in Europe before this date and Hirsch states that the earliest information concerning epidemic icterus comes from Minorca, where the malady was prevalent during July and August 1745.

Cockayne (1912) was the first to distinguish between Weil's disease and what he called "epidemic catarrhal jaundice". Since then a number of outbreaks of the latter have been recorded, particularly during the past decade. It is probably true to say that the various outbreaks described as "acute infective jaundice", "epidemic catarrhal jaundice", "common infective jaundice", "infective hepatic jaundice", "mild hepatic necrosis", and now "infective hepatitis" are synonymous and do in fact refer to variants of the same disease, chiefly in connexion with the symptomatology.

Since the beginning of 1936 I have kept detailed records of all cases in Leicestershire which have been reported by general practitioners, health visitors and school teachers, but as the disease is not compulsorily notifiable the figures are incomplete. Details of the first outbreak which I investigated were published in 1937; this was the second to be recorded from the county. The survey includes both the data collected at that time and the details published by Montford in 1934.

Incidence.—In the Castle Donington outbreak of 1933, Montford records that 45 cases in all occurred between February and September of that year. Of this total 21 cases were patients of a neighbouring practitioner and of these no details are given. The remaining 24 cases were evenly distributed between the sexes, and, with two exceptions, all were children. There were no deaths.

I have failed to trace the occurrence of any cases of infective hepatitis in the county between 1933 and 1936.

DISTRIBUTION OF CASES
OF INFECTIVE HEPATITIS
IN LEICESTERSHIRE —
1936–43.

KEY TO EPIDEMICS

1936—7 ———
1937—8 ———— ▲
1938—9 ———— +
1941—2 ———— ○
1942—3 ———— ■ ●

SCALE

MILES

N

MONTHLY INCIDENCE OF INFECTIVE HEPATITIS
IN LEICESTERSHIRE.
1936-43

CASES

132
120
108
96
84
72
60
48
36
24
12
0

MONTHS 1936 1937 1938 1939 1940 1941 1942 1943
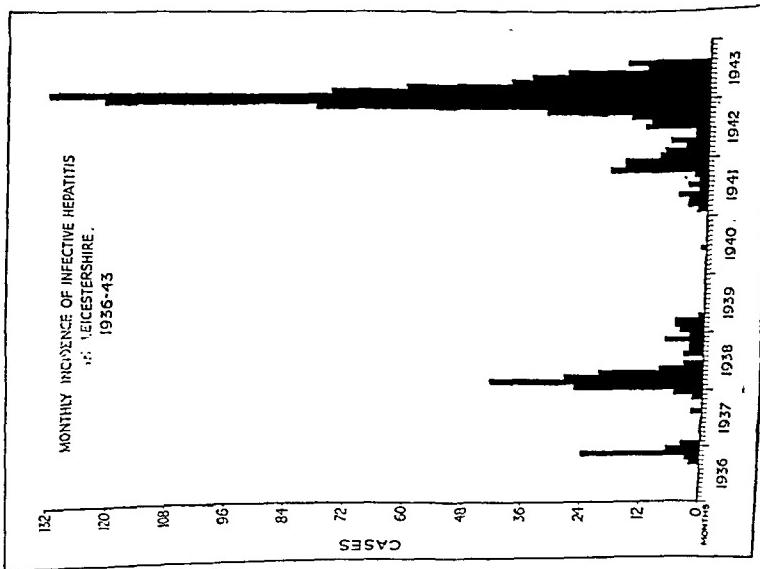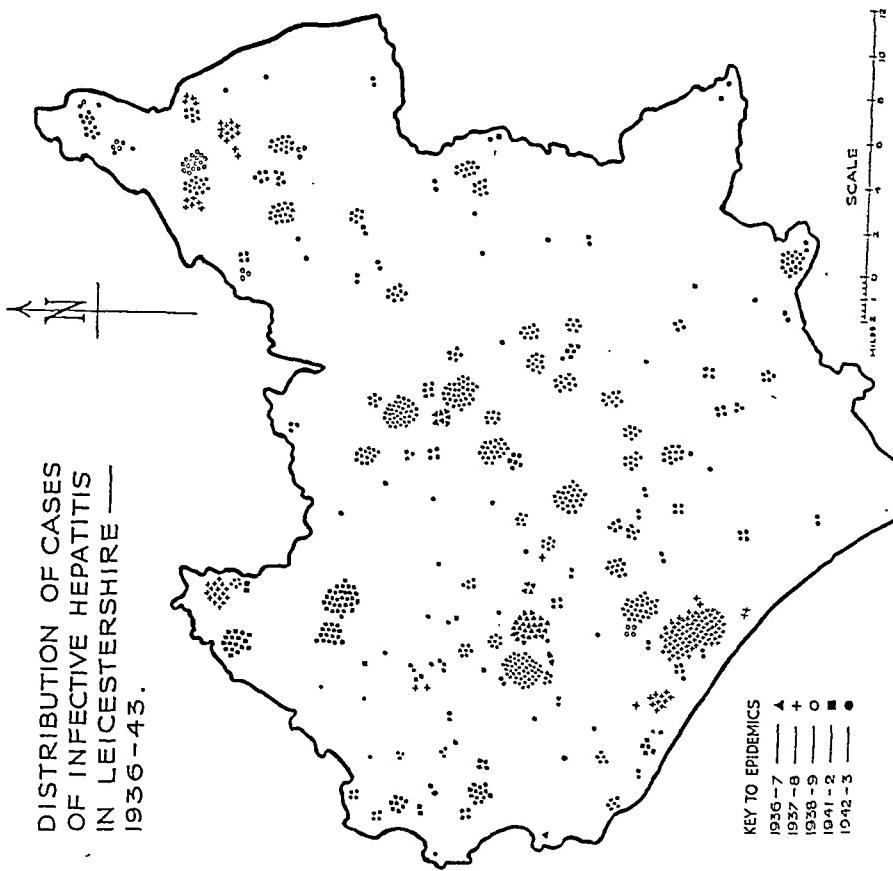
From the beginning of 1936 careful records have been maintained and 1,017 cases have been investigated; it is estimated that they represent about 80% of the total number of persons who contracted the disease. These cases can be grouped into five separate epidemics, all more or less typical in character, and each reaching the peak during the winter months as illustrated in the graph. Thus the seasonal incidence is typical of this disease.

In the last epidemic of the series infection was scattered over the county, with more cases in some areas than in others, but without any relationship to population. Though outside the scope of this survey, it is worth noting that during this epidemic a number of cases also occurred in Leicester City and three of these, two children and one adult, died between October 28 and November 14, 1942. The death of another adult which took place between these two dates may also have been due to infective hepatitis.

It was often difficult to trace a connecting link between outbreaks in isolated villages, but having in mind that in all parts of the county senior school children are conveyed daily to and from central schools, and also in view of the increase in industrial employment, particularly during the war, the possibility of infection occurring simultaneously in a number of widely separated areas appears more obvious.

Tracing the serial infection of cases, so typical of this disease, is often rendered more difficult by the fact that a number of subclinical or abortive cases occur, many of which are undoubtedly missed. In these cases the symptoms are mild and usually jaundice is absent. The family doctor or district nurse is not therefore consulted and thus such cases do not come to our notice. It is because of these missing links that the chain of evidence supporting a case-to-case spread is often broken, and leads observers to doubt serial infection and to infer that the disease is spread by water, milk, food, or other vector.

The age-sex incidence, as shown below, agrees with the findings of other observers in that it is evenly distributed between the sexes, with the age incidence highest in children between 5 and 10 years.

TABLE I.

Epidemic	Number of cases			Age distribution							
				0—5		5—10		10—15		15 and over	
	Male	Female	Total	No.	%	No.	%	No.	%	No.	%
Sept. 1936–Jan. 1937 ...	19	21	40	5 .	12·50	29	72·50	6	15·00	—	—
Aug. 1937–June 1938 ...	78	63	141	7	4·96	76	53·90	46	32·62	12	8·51
Aug. 1938–April 1939 ...	19	20	39	5	12·82	18	46·15	9	23·08	7	17·95
Feb. 1941–June 1942 ...	55	64	119	8	6·72	72	60·50	34	28·57	5	4·20
July 1942–Aug. 1943 ...	334	343	677	40	5·91	288	42·54	269	39·73	80	11·82
Totals ...	505	511	1,016	65	6·40	483	47·54	364	35·83	104	10·24

The above table does not include one isolated case which occurred in June 1940 and proved fatal.

The migratory character of the disease during epidemics is well illustrated in the accompanying outline map showing the distribution of cases in Leicestershire since January 1936.

There are two distinct types of local outbreak in town or village—one in which a number of cases occur within a short period of time and another in which the incidence extends over a much longer period. Why the disease should exhibit these two characteristics is open to speculation. Probably many factors are involved, the most important being the degree of immunity of the local population.

Ætiology.—Careful investigation failed to produce any conclusive evidence that infection was spread by such agencies as milk, water, food or vermin. On the contrary the absence of the explosive appearance of cases over areas corresponding to the distribution of milk, water or food from a common source, and the case-to-case spread of infection which could be traced in most districts, both appear to prove that the disease is transmitted from patient to patient by direct contact, probably by droplet infection.

An incubation period of approximately one month was estimated by studying the early cases, which agrees with the reports of others, particularly Pickles (1939b), who has gone to great length to prove that the incubation period almost certainly extends to between twenty-six and thirty-five days.

The period of infectivity is not so certain but from evidence arising from this investigation the patient is probably infectious for at least a week before the appearance of jaundice, after which infectivity apparently ceases.

Clinical features.—Throughout the whole series of cases the clinical features remained remarkably constant. There was always a sprinkling of more severe cases in which all the symptoms were more marked, and in several instances small groups of such cases would appear together in a circumscribed area. At the other end of the scale a larger number of mild or abortive cases could be traced in which all the symptoms were of a very mild and transient character or, what was more usual, only some of the symptoms were present. Often there was no trace of jaundice whatever, or jaundice would be present but only detectable in the conjunctivæ, and the fæces and urine would remain

normal; more rarely none of these symptoms was apparent but the patient would give a history of having vomited once or twice, or of having had a feeling of nausea with anorexia and perhaps headache.

. It is the latter type of very mild or abortive case which, as pointed out above, causes difficulty in filling in the background of an epidemic. Cullinan (1939) points out that unexplained gaps which sometimes appear in epidemics may indicate the presence of carriers.

Some epidemics are characterized by the appearance of unusual symptoms, and the following table gives the incidence of those which occurred in the five outbreaks under discussion.

TABLE II.

Epidemic		No. of cases	Coryza		Sore throat		Rash		Epistaxis	
			No.	%	No.	%	No.	%	No.	%
Sept. 1936–Jan. 1937	...	40	—	—	1	2·5	—	—	—	—
Aug. 1937–June 1938	...	141	46	32·62	19	13·48	1	0·71	—	—
Aug. 1938–April 1939	...	39	10	25·64	5	12·82	—	—	—	—
Feb. 1941–June 1942	...	119	49	41·18	12	10·08	—	—	2	1·68
July 1942–Aug. 1943...	...	677	292	43·13	94	13·88	35	5·17	8	1·18
Totals	... ...	1,016	397	39·07	131	12·89	36	3·54	10	0·98

The rash in the majority of cases was urticarial in character, but there was no correlation between this type of eruption and the severity of infection. In contrast, the few cases of morbilliform or petechial rash which were observed, were confined to the more severe type of infection. Montford records one case of morbilliform rash in his series.

In a typical case of moderate severity the onset is gradual and for a period of several days before definite symptoms develop there is general malaise, headache, anorexia and perhaps nausea; more rarely coryza or sore throat is present. There is often a slight rise in temperature, but in some cases though the face is flushed the temperature is found to be normal. Bradycardia is frequently present.

The prodromata are quickly followed by pain in the upper abdomen, usually accompanied by vomiting. Both last for a short time and are followed by tenderness in the epigastrium which persists for some days. At this stage enlargement of the liver is elicited in many cases and more rarely some enlargement of the spleen also. From one to fourteen days after the acute symptoms develop jaundice appears, usually starting in the conjunctivæ and spreading over the face, neck, arms, trunk and lower limbs. At the same time the fæces become pale and urine dark, though these latter symptoms may precede the appearance of jaundice by a short period of time. *Jaundice attains its* maximum intensity in two or three days and usually lasts from about seven to ten days. Where jaundice has been widespread and deep in colour, itching frequently occurs. Recovery is usually slow and convalescence is complete in from two to four weeks, but may take longer.

In severe cases all the symptoms are exaggerated, jaundice is deep in colour and covers the whole body and the epigastric pain may be so severe as to simulate an "acute abdomen". Those cases in which jaundice is very intense exhibit a peculiar orange flush of the face; pigmentation persists for longer than usual, and in one case was still present at the end of eight weeks. As a rule one finds the disease more severe in adults and complete recovery more protracted.

Four instances of a second attack and two of relapse are recorded:

Second Attack:
    (a) Male aged 6 years ... ... Onset February 1938 and May 1938.
    (b) Male aged 9 years ... ... Onset August 1937 and April 1942.
    (c) Female aged 10 years ... ... Onset February 1943 and August 1943.
    (d) Female aged 13 years ... ... Onset August 1942 and June 1943.

With the exception of the first case the symptoms in each instance were more acute during the first attack.

Relapse:
    (a) Female aged 5 years ... ... Onset January 1942 and February 1942.
    (b) Female aged 9 years ... ... Onset December 1942 and January 1943.

In both cases the symptoms were more acute during the recrudescence; the first case terminating in death.

Complications.—Complications are said to be very rare. Cullinan (1939) refers to a case of parotitis reported to him in a personal communication by Glover, and Martland and Winner (1939) record one case of oophoritis.

In the cases under review I believe there is good evidence that the pancreas may be affected in this disease, as I can record two cases in which diabetes followed almost immediately after an attack of epidemic jaundice. Chronic pancreatitis was noted in one of the fatal cases during an exploratory laparotomy. The severe epigastric pain which accompanies so many cases indicates that mild attacks of acute pancreatitis may be a relatively common complication. An involvement of the pancreas is suggested by the occurrence of persistent intermittent glycosuria in three other cases.

Mortality.—It is impossible to make any categorical statement concerning the mortality due to infective hepatitis during the period covered by the investigation. Three deaths certainly occurred, a child and two adults; and there is circumstantial evidence that at least two other adults died as a result of this disease. The difficulty lies in the fact that in adults organic disturbances often persist long after the initial attack of jaundice has subsided and has been almost forgotten by the patient. Thus by the time admission to hospital takes place attention is focused on the existing symptoms, while the attack of jaundice which occurred some weeks or even months earlier is not regarded with the signifi-cance it deserves, and the contemporary epidemic, which has probably subsided by this time, is more than likely overlooked altogether.

The following are details of the only fatal case for which a post-mortem report is available:

Female, aged 5. A robust child, always in good health. On January 23, 1942, her mother noticed that the child was sleepy, listless and had a poor appetite. Shortly afterwards she vomited on several occasions and on 26th the conjunctivæ were jaundiced but pigmentation was not apparent elsewhere. At the same time the motions were pale and the urine dark. The child quickly recovered and returned to school.
On February 21, 1942, the symptoms returned but were much more severe, particularly vomiting. Epigastric pain, which was absent in the first attack, was intense and the child also complained of severe headache. Jaundice appeared again on 23rd and quickly became generalized and deep in colour. Acute spasms of abdominal pain persisted and on March 3 and 4 ·meningeal symptoms, in the form of convulsions, developed with epistaxis. The child was admitted to hospital on March 5 where a lumbar puncture was performed but the specimen of fluid examined was normal.
The child died on March 6 and the following are the details of the autopsy: Brain: Dura stained; convolutions flattened; clot of blood round hypophyseal stalk. Lungs: A few scattered hæmorrhages, otherwise normal. Heart: 2½ oz., normal except for hæmorrhages both pericardial and interventricular. Peritoneum: Numerous hæmorrhages in the great omentum, mesentery and on the posterior abdominal wall, and extensive hæmorrhages in the areolar tissue surrounding the kidneys and suprarenals. Glands: Enlargement of mesenteric glands, only two of which are tuberculous (caseous). Kidneys: Capsule strips readily and well-marked cloudy swelling of the cortex which stands out in marked contrast to the red medulla. The cortex looks yellow, opaque and has lost its normal pattern. Liver: 15 oz., flabby and jaundiced throughout with occasional hæmorrhages. Spleen: 2½ oz., appears slightly enlarged. Suprarenals and remaining organs normal. Gall-bladder: Contains greenish slimy bile. No pus cells and no organisms. No pigment deposit and quite clean. A well-developed child whose skin shows well-marked jaundice with bright malar flush. A few blotchy skin hæmorrhages. Death due to epidemic catarrhal jaundice.

Laboratory investigation.—In the first group of cases which I investigated, blood serum tested for agglutination against the following, proved negative in all dilutions: *B. typhosus* H and O, *B. paratyphosus* A and B, *B. dysenteriæ* Sonne, *B. dysenteriæ* Shiga, *B. dysenteriæ* Flexner, *B. aerirycke*, and *B. abortus* Bang. A series of blood films was also made and as is usual in epidemic jaundice a monocytosis was evident, varying from 2 to 19%.

Random specimens of urine were collected throughout the whole series for examination so as to rule out the possibility of Weil's disease but no spirochætes were found. Specimens of fæces were also examined for abnormal bacteria but without result.

When it was ascertained that an epidemic had commenced in the autumn and winter of 1937-38, I supplied Dr. G. M. Findlay of the Wellcome Bureau of Scientific Research with nasal washings and specimens of blood and fæces from cases in the pre-icteric stage. Families in which one or more cases of jaundice had occurred were chosen and specimens were taken from contacts, most of whom developed jaundice in due course.

Dr. Findlay inoculated monkeys, rats, mice, cats, dogs, ferrets and guinea-pigs without result. He also endeavoured to obtain a growth on the developing chick embryo, but without result.

Differential diagnosis.—Infective hepatitis has many synonyms, and when investigating an epidemic of jaundice it is only necessary to exclude Weil's disease by animal inoculation of a centrifuged deposit of blood or urine.

Treatment.—There is no specific treatment for infective hepatitis. Treatment chiefly consisted of confinement to bed for a few days and the relief of symptoms.

It was not considered that any useful purpose would be served by closing the schools

affected, but children, who had been in close contact with this disease, and who attended senior schools some distance from their home village, were excluded for several weeks. It is doubtful, however, if this had any appreciable effect on the incidence of infection in the county.

SUMMARY AND CONCLUSIONS

(1) A total of 1,062 cases of infective hepatitis have been investigated in Leicestershire, including 45 cases recorded by Montford (1934). It is estimated that the 1,017 cases investigated between January 1, 1936, and August 31, 1943, represent approximately 80% of the cases which occurred during the same period.

(2) Although the two epidemics previously described from this county were referred to as infective hepatic jaundice and epidemic catarrhal jaundice respectively, there is overwhelming evidence that these and other descriptions are synonymous.

(3) Two distinct types of local outbreak are noted. The first in which the cases occur over a short interval; the second, and more usual, in which the cases are spread over a much longer period.

(4) Many of the findings agree with those described by other observers. Thus:
   (a) The majority of cases occur in children of the 5 to 10 age-group, and the sexes are equally affected. Seasonal incidence is also typical.
   (b) Infection is spread by close personal contact, probably by means of droplet infection.
   (c) The incubation period averages four weeks. Infectivity is probably at its maximum for at least a week before jaundice appears, but almost certainly disappears at the icteric stage.
   (d) There is no evidence that infection is spread by means of milk, water, food or vermin.

(5) Four instances of second attacks and two of relapse are noted.

(6) There is evidence that attacks of infective hepatitis may be followed by diabetes, intermittent glycosuria and pancreatitis, complications not hitherto described as far as can be ascertained.

(7) Three cases terminated in death, but it is possible that other fatalities also occurred due to this disease. Details are given of an autopsy on one case.

(8) Attempts during the 1937-38 epidemic to isolate the causal organism by the Wellcome Bureau of Scientific Research, from material supplied, were unsuccessful.

I am indebted to Dr. J. A. Fairer, county medical officer of health, for giving me every facility in carrying out the survey; also to the many general practitioners, the health visitors and school teachers who co-operated in the field work.

BIBLIOGRAPHY

COCKAYNE, E. A. (1912) *Quart. J. Med.,* 6, 1.
CULLINAN, E. R. (1939) *Proc. R. Soc. Med.,* 32, 933.
DIBLE, J. H., McMICHAEL, J., and SHERLOCK, S. P. V. (1943) *Lancet* 949, 402.
EDWARDS, L. R. L. (1943) *Brit. med. J.* (i), 474.
EVANS, P. (1942) *Brit. med. J.* (ii), 446.
GRAHAM, G. G. (1938) *Lancet* (ii), 1.
HARRIES, E. M. R., and MITMAN, M. (1941) Clinical Practice in Infectious Diseases, Edinburgh.
HIRSCH, A. (1886) Handbook of Geographical and Historical Pathology, London.
LISNEY, A. A. (1937) *Brit. med. J.* (i), 703.
MARTLAND, E. M., and WINNER, A. L. (1939) *Lancet* (i), 161.
MINISTRY OF HEALTH, Memorandum prepared by Medical Officers of (1934) *Lancet* (i), 88.
MONTFORD, T. M. (1934) *Brit. med. J.* (i), 330.
NEWMAN, J. L. (1940) *Med. Offr.,* 64, 21.
 —— (1942) *Brit. med. J.* (i), 61.
NICOL, C. G. (1942) *Brit. med. J.* (i), 466.
PARSONS, F. B. (1939) *Proc. R. Soc. Med.,* 32, 1197.
PICKLES, W. H. (1939a) *Lancet* (i), 893.
 —— (1939b) Epidemiology in Country Practice, Bristol.
PROPERT, S. A. (1938) *Brit. med. J.* (ii), 677.

Dr. J. C. Ford: Infective hepatitis is believed to have been endemic in the south-west corner of the borough of Wembley for some time: it spread slowly in that area and in a nearby district from July to September 1942, and then reached the north and north-east areas in October, where it spread much more rapidly. The peak incidence was in January 1943, with 102 cases reported in that month. In all, it is known that well over 300 cases occurred before the epidemic was over. The rate of spread across the borough was approximately the same as that of virus infections such as measles.

It was noteworthy that the communities most heavily attacked were those of artisan class, while flat-dwellers, and the better-class districts were singularly free.

The major part of the borough receives its water supply from a single source, and in view of the above remarks, water can be excluded as a cause of the spread.

The incidence fell most heavily on children of school age, and especially those in two schools in the north and north-east areas. In one of these there were 78 cases out of 778 children on the registers. No explanation has been offered as to why this school was singled out.

The clinical features resembled those reported by other observers.

Dr. J. L. Newman: In a South London Day Nursery in the autumn of 1938 one young adult attendant fell ill with hepatitis. No further particulars are available until about May 28, 1939, when two other attendants succumbed. In June a fourth attendant, Miss N., began a typical attack. As far as could be found out afterwards there were no known cases of hepatitis among some 40 children in the nursery throughout this period.

In August the Nursery with 25 children was evacuated to Sussex to the home of Miss N. On the 31st she went bathing, was cold and began what she thought was a recurrence of jaundice but without turning yellow: her urine was "dark". That it was hepatitis is fairly certain because some forty days later five persons were taken ill with typical attacks, three on October 10, one on the 11th, and the fifth on about the same date. The persons concerned were an inmate of the Nursery: Miss E., attendant aged 19, and three relatives of Miss N., two being adult females and one a schoolboy who had returned to school on September 29. The attacks were typical and there were no others in the Nursery, abortive or otherwise. On about October 14 a Mrs. W., aged 54, was taken ill with hepatitis at a cottage in the village. One fact about her was that she had been an invalid for three years following an abdominal operation, and was positive that she had not been out of the house for months. No direct contact could be established between this patient and any of the others, but her son aged 15 worked as cowman-gardener at the N.'s house.

The interesting features of this small outbreak were, first the apparent relative immunity of the children at risk, and, second, the part played by the healthy person. In Miss N.'s case, the noxa of hepatitis seemed to lie dormant but potentially active for over two months. In Mrs. W.'s case, an uninfected person seemed to be capable of conveying the infection.

Dr. Eli Davis (*L.C.C.*): 29 cases were admitted to hospital between October 1942 and October 1943. All were children and young adults, and included three pairs of siblings. Acute appendicitis was the original diagnosis in three cases. One nurse who was treating some of these jaundiced patients developed the disease. We had under our care a patient with long-established acholuric jaundice, and two of his maternal cousins (not siblings) developed infective hepatitis. A number of these patients came from the Isle of Dogs—mentioned by Dr. Brincker (in the Chair) as an endemic area for infective hepatitis.

The 1942 Epidemic of Infective Hepatitis in the Middle East

Dr. E. T. C. Spooner (*Emergency Public Health Laboratory Service, Cambridge*): This report was collected from many observers in the Middle East last year by No. 1 Medical Research Section. We were particularly indebted to Colonel A. E. Richmond, D.D.H., M.E.F., and his staff, and to many medical officers in hospitals, in P.O.W. camps and in individual units, as well as to a large number of non-medical officers whom we questioned.

By reason of other work, we were unable to start collecting information until the epidemic had passed its peak. A trained epidemiologist investigating the disease in the field while the epidemic was in progress might have gone much further.

The events of the two previous years and the record of the last war as told in the Medical History of the War, had made it possible to predict the 1942 epidemic of infective hepatitis, but I do not think that anyone could have foreseen that it would be of such magnitude.

In the 1942 epidemic there was a very abrupt rise in incidence in October, with further rises in November and in the peak month of December. Both in 1941 and 1942 the jaundice season coincided with the season of winter fighting.

The brunt of the Middle East epidemic was borne by the Eighth Army. Over a quarter of the total cases in the Middle East came from the Eighth Army. In December, when the case rate per thousand per month for British and Dominion troops was nine for the whole period, the incidence among Home Forces did not rise above 0·2 per thousand. There were many examples in the Eighth Army of regiments in which 8% or 9% of the total strength went down with infective hepatitis, this figure often including up to a third of the regiment's officers, for officers were about 4·7 times as prone as other ranks.

The main epidemic started with the 2nd New Zealand and 9th Australian Divisions, reaching its maximum among these in early October. Both of these divisions had spent the summer in the Alamein line, the Australians at the extreme north of it on the coast, and the New Zealanders in the Central Sector. Much of the Alamein line was very dirty, with abundant flies and imperfectly buried corpses in the neighbourhood. In the second week of September, the New Zealand Division moved out of the line to a rest position in a clean piece of desert near Wadi Natrun. While they were in this position, their main epidemic developed: it had passed its peak by the time that they moved up into the line again for the battle of October 23.

In many of the British units, the peak of the epidemic came later. For example, in the 51st (Highland) Division, incidence rose steadily from early September to a maximum in the latter half of December. It was noticeable that the epidemics in the smaller units constituting this division, showed curves which resembled one another and corresponded to that of the Division as a whole.

Several British regiments which went into the Alamein line shortly before the October battle and retired to rest positions in the Delta in mid-November, to camps which had been almost empty during the previous few months, also developed their epidemics after leaving the line. It appeared that a period of residence in the Alamein line might be a predisposing cause of the epidemic. Unfortunately, it was not possible to collect enough histories of individual units to test this hypothesis very thoroughly. It is supported by the histories of ten field regiments, R.A., although their moves during the relevant period were so complex as to make interpretation very difficult. Two of these regiments landed in the Middle East in September or early October after a jaundice-free voyage. They spent a short time (ten and thirty-seven days respectively) training and equipping themselves in the Canal and Delta areas, and then went to the Alamein line in mid-October for the battle, and fought until the end of the first week in November, when, after a short rest in the desert, they returned to clean base camps in the Cairo area. Both of these regiments had their main epidemics after returning to the Delta, about a month after the battle.

The story of the armoured brigades also suggests that residence in the desert helped to determine the magnitude of the jaundice epidemic. The incidence in four brigades which spent the summer in the Delta was considerably lower than that in three others which spent the summer in the desert.

Although it appears that those units which spent the longest time in the desert or the Alamein line were the most heavily affected, one must be careful not to exaggerate the point. During December, when the case rate per thousand per month for the Eighth Army was 15 for British and Dominion troops, the corresponding figure in Syria was 9.

No definite information concerning the length of the incubation period of the disease was obtained. No special occupation was associated with either a high or a low incidence; except that, as already stated, officers were about 4·7 times as prone as other ranks. This was apparently true also of the Italians. No explanation can be offered for the higher liability of officers; but in this connexion it has been pointed out that we have very little information about the relative proneness of officers and other ranks to diseases other than infective hepatitis.

A definite racial variation in susceptibility was revealed, in that Indian troops and Maoris, although both occasionally developed the disease, were very much less frequently attacked than were Europeans.

There were no good grounds for suspecting an insect vector: except that flies, which are nowhere rare in the Middle East, were particularly abundant in the Alamein line in October and November.

No direct evidence was obtained concerning the means of spread of the disease, but two observations cast some doubt on the hypothesis of droplet infection. One was that in units which lived by vehicle crews, there did not seem to be any special tendency for more than one case to occur in the crew of one vehicle. In four tank regiments, with a total of 106 cases between them, there was only one instance of two cases occurring in the crew of the same vehicle. In one field regiment R.A. in which there were 59 cases, there were 8 instances of more than one case occurring in the crew of a vehicle, but in most of these the time interval between the onset of cases in the same vehicle was a fortnight or less.

The other observation which seems inconsistent with a droplet spread was that the disease showed curiously little tendency to spread from prisoners of war captured in November, among whom jaundice was rife, to others who shared the same camps and even pens, but who had been captured in the previous spring and summer. Two P.O.W. camps were visited and studied with this question in view. At one there were 14 cases of jaundice among 2,000 "old" prisoners captured in the previous July. Seven of these cases developed before November, and seven during and after November, at the beginning of which month about 8,000 newly captured prisoners were admitted to the camp. Among these "new" prisoners, there were 272 cases of jaundice. All of these prisoners, both old and new, were Italian other ranks.

In the second P.O.W. camp, also for Italians, there were in early November 500 "old" prisoners, other ranks who were retained in the camp to wait on incoming captured Italian officers, and who had been in the camp throughout the summer. In November, 1,120 newly captured Italian officers were admitted, 101 of whom subsequently developed jaundice. None of the 500 "old" prisoners who waited upon them contracted the disease.

Section of Odontology

President—HAROLD CHAPMAN, L.D.S.Eng.

[*October* 25, 1943]

Prognosis in Orthodontics

PRESIDENT'S ADDRESS

By HAROLD CHAPMAN, L.D.S.Eng.

(*Dental Surgeon to the London Hospital.*)

ONE of the most important aspects of orthodontic treatment to-day is prognosis, which may be defined as the knowledge of what movements of teeth and jaws will be permanent after, say, three years' treatment, sometimes longer, sometimes less.

The dental profession and the public have such confidence in our ability to obtain a perfect result in every case that it is embarrassing to have to explain that in many a compromise is the only solution.   By perfect result is meant one which is permanent and leaves nothing to be desired as regards alignment and occlusion: the two latter are frequently obtainable but their permanency cannot be judged till appliances have been discarded several years, when the ultimate result will be apparent.   It is this ultimate result which is so important: unfortunately it is rarely available to the specialist orthodontist, who has to rely on fortuitous circumstances to bring it to his notice.   This is a reason why it requires the combined resources of many practices to accumulate the records from which to draw conclusions; it is more likely that these records will be forthcoming from private practice than from any form of public orthodontic service.

The study of these ultimate results is valuable in that we learn from them what is the best treatment for any particular case.   I have been able to collect some such records and have supplemented them by others from which conclusions can be drawn (*see* illustrations).

Much orthodontic literature gives the impression that the perfect result can always be attained.   Though this may be so in many cases there are numerous exceptions.   In some the perfect result can be obtained but not retained, and sooner or later relapse occurs, undoing years of work.   How much better for patients and profession to recognize these exceptions and to adopt what may be called a compromise treatment that will be both beneficial and permanent, æsthetically and functionally, though falling short of the elusive perfect result.

One frequently hears criticism of a compromise treatment, involving, say, the loss of an upper incisor, as if it were unwarranted.   Actually it may be the best solution in the circumstances though the implication is that something better could have been done.   The critics, however, overlook the fact that the *immediate result*, however excellent, may not be permanent and that our aim must be an *ultimate result* showing a definite and lasting improvement on the original condition.   The result which is permanent is the better though it fall short of perfection, but it must satisfy æsthetic and functional demands in so far as the original condition permits.   This latter is so variable in degree that it is unreasonable to expect an equally good permanent result in every case.

Cases of relapse are not uncommon and reflect no credit on the practitioner. They are best avoided by adopting a type of treatment with a good prognosis. If this is not possible, it is better not to begin treatment. This orthodontic problem, entirely different from any other in dentistry, requires all one's care and ingenuity for its solution, bearing in mind that it is not sufficient to align and occlude teeth but the teeth must *remain* in alignment and occlusion. If I cannot foresee a reasonable degree of permanent improvement, I prefer not to undertake a case. While it is not possible to eliminate all failures they should be reduced to the minimum. Failures in orthodontics are an enormous waste.

Experience alone teaches what type of treatment will be successful; it is a matter of trial and error. The combined experience of many should be available to enable each practitioner to say what procedure will be beneficial. Few practitioners have published ultimate results, but from time to time one comes across straws which show the way the wind is blowing. These may advise something other than the usual directions for tooth movement, thus suggesting that previous directions of movements had not given the desired result, or they may be the confessions of an unusually communicative orthodontist. Reading between the lines one concludes that it is not possible, in every case, to keep all the teeth and get a good result. From this it would appear that treatment must not be based on theory or research alone, but also on clinical experience: new methods of treatment must bear the test of clinical experience before adoption as a routine. This test takes years in some instances, yet one hears of new treatments being praised after a brief trial.

Research workers have added to our knowledge of many aspects of orthodontic practice, e.g. the effect on the bone of force applied to teeth may cause it to be absorbed in some areas and deposited in others, but one is forced to the conclusion that such changes may not be permanent or the relapses known to every orthodontist would not occur. This simple illustration is given to emphasize that clinical results, obtained in actual practice and not effects seen in the laboratory, are the basis for orthodontic treatment: all new methods of treatment must be studied critically, and it must not be assumed that all are advances.

Illustrations of five cases are used to amplify the text; they are arranged according to (Angle Classification) arch relation, and are described in the legends. The important points are:

Class I: In those cases in which the arches are not large enough for the teeth, extraction of upper teeth is essential because the bones cannot be enlarged. Prognosis is unfavourable if all the teeth are kept, though it is often necessary to compromise as regards the lower teeth and to leave them in their original state.

Classes II and III: Prognosis is favourable for the correction of the position of the mandible: if the arches are too small the considerations as for Class I apply in addition.

In some cases of Class III type in which the error is slight and the maxilla relatively smaller than the mandible, the prognosis is not so good as in true prenormal occlusion.

All cases with good arches, which implies normal-sized maxillary bones, give better results than cases with small arches.

The prognosis as regards errors of individual teeth is uncertain but usually the earlier these are corrected the better.

The first case was a typical Class I (Angle) small arches in normal relation (boy), treated by enlarging the arches at age 7 years 8 months, showing a good result at age 13 years 10 months, but considerable relapse at age 29 years. There is no record of the condition between 14 and 29 years. This case has already been published in the *Transactions* of the British Society for the Study of Orthodontics, 1938, p. 23.

Fig. 1.—No. 3246. Male, aged 12 years 6 months: Diagnosis—Small arches in normal relation. 2 | diminutive: extracted. 1 | 12 have been moved to the right. 3246 A, the same case aged 14 years 6 months. If 2 | had been a normal tooth but rotated, prognosis would be best if it or | 2 had been removed. No treatment—not even extraction—advised for lower arch. Loss of 6 | may allow arch to contract a little; this may not be harmful as there is slight spacing of the upper teeth. Prognosis good.

Fig. 2.—No. 1527. Female, aged 7 years: Diagnosis—Class II, Division I. Good lower arch.

Aged 7 years 8 months: Treatment begun with fixed appliances and intermaxillary traction to bring the mandible forward.
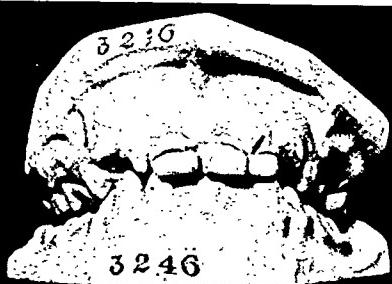
3246. M . 12 — 6.   FIG.1   3246 A.   M.14 — 6.

1527.   F. 7 - O.

1527C.   F.11 — 4.   FIG.2.   1527F.   F.22 — 1.

3198A. F. 8-4.   3198B.F.10 — 7.

FIG.3.
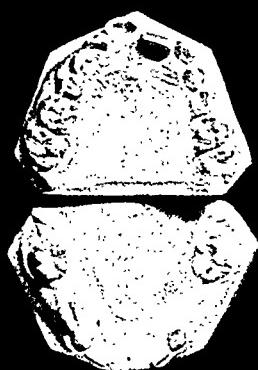
L.H. 996. F. 7–10. L.H. 996A. F. 9–4.
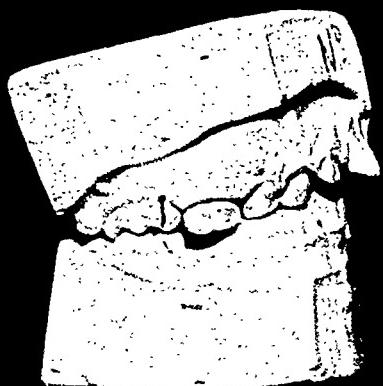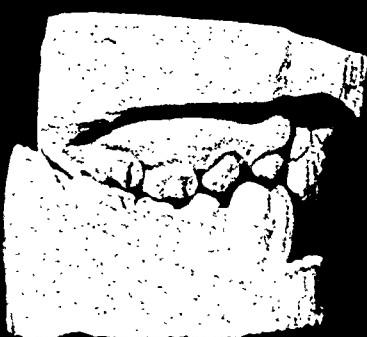
L.H. 996 F. 7–10. L.H. 996A. F. 9–4.

FIG 4.

3264 3264B

3264 .F .4 –11. 3264B. F. 6–7.
FIG. 5. FIG. 5. B.

Aged 8 years 11 months: Upper appliance left off for five months with little or no relapse. Lower appliance left in to keep pre-molar spaces.

Aged 11 years 2 months: All appliances removed.

Aged 11 years 4 months: Put in vulcanite retention plates for night wear with inter-maxillary traction; patient was conscientious about this at first but did not wear them continually for long; probably worn in all for six months spread over two years; they were not worn for weeks at a time. Model 1527 c.

Aged 22 years 1 month: Model 1527 r shows post-normality corrected, slight imbrication of upper and lower incisors. Prognosis good.

Fig. 3.—No. 3198 A. Female, aged 8 years 4 months: Diagnosis—Class II. Division I on right, Division II on left.

Aged 8 years 5 months: Treatment begun with fixed appliances and intermaxillary traction to bring the mandible forward: |1 moved labially into line with 1 |.

Aged 10 years 7 months. Models two years two months after treatment was begun. Appliances removed.

Aged 10 years 10 months: No relapse: appliances replaced for retention. Prognosis probably good.

Fig. 4.—No. L.H. 996. Female, aged 7 years 10 months: Diagnosis—Class II. Division I on right, Division II on left. Good lower arch, 2| rotated. |1 in good relation to lower teeth. Post-normality half a cusp bilaterally.

Aged 7 years 10 months: Treatment—Extract 2| ; retract 1|2 and move 1| to the right.

Aged 9 years 4 months: Models. Retention with plain band on |1 carrying labial spurs 1|2.

A suitable case for this simple method of treatment in which the position of the mandible has not been changed. Uncertain how long retention will be required and how perfect the alignment will remain; if there is relapse it is the disadvantage of this method of treatment. Prognosis probably good.

Compare case No. 3198 (fig. 3) in which the instanding central was moved labially into line with the other and the mandible moved forward; this acts as a retainer for the labially moved central and so relapse of incisor alignment is unlikely. This case is not so favourable for treatment with extraction as is case No. L.H. 996 (fig. 4). Neither case has been under observation long enough to speak of the long-term results but both methods of treatment seem to have a place.

Fig. 5.—No. 3264. Female, aged 4 years 11 months: Diagnosis—Arches (probably) good. a | abc lingual to lower teeth. Pre-normal occlusion of lower arch with deviation to the left. Profile has slight suggestion of Class III. a|a show signs of attrition on their labial surfaces.

Aged 4 years 11 months: Head and chin cap with intermaxillary traction to retract the mandible for wear both night and day. Lower plate with shod incline to assist a|a labially.

Aged 5 years 1 month: a|a correct. cb|bc not quite enough labial.

Aged 5 years 1 month: cba|abc correct. Gradually reduced wearing of plate and head and chin caps until

Aged 5 years 4 months, when instructed to discard all appliances.

Aged 6 years 7 months: Occlusion excellent. Are the arches large enough? Case to be watched for this. Case corrected in three months; appliances discarded in five months. Prognosis excellent.

The cases illustrated bring out the great value of intermaxillary traction, but it involves operative procedures which have restricted its use: its value is undoubted and before other methods replace it on a large scale, one must make sure that they have definite advantages: to decide this will take years of clinical work and observation. Therefore, sudden and spectacular advances in treatment are not to be expected, particularly of those irregularities—post-normal and pre-normal occlusion—which are often deformities and form such a large part of a specialist's practice. It is well to remember that the incidence of caries is not likely to fall during the progress of orthodontic treatment.

To ensure the best results for the patient, orthodontic and conservative work must be done in close co-operation. As the practice of orthodontics increases, prognosis becomes

even more important, not only from the point of view of permanency of result but also in selecting the method of treatment. In order to foresee the ultimate result before treatment is begun prognosis must be known and acted upon. It is often easy to produce what appears to be a brilliant result but which may be as transient as a rainbow. Appliances are important but if the result they produce is not permanent, it matters not how perfect they are.

[The text has been abbreviated and seven of the cases shown, omitted; four of these showed long-term results.]

Mrs. Lilian Lindsay, L.D.S., described a case of Bell's palsy in two sisters. It was congenital in both and appeared to be hereditary, as it would appear from a photograph of the father of the girls that he had the same condition.

Section of Laryngology

President—W. M. MOLLISON, M.Ch.

[*November* 5, 1943]

DISCUSSION ON PAIN IN LARYNGOLOGY

PRESIDENT'S ADDRESS

By W. M. MOLLISON, M.Ch.

IN laryngology the position of pain is sometimes a guide to the affection of the under-lying tissues but often this is not so, the pain being referred remotely. Sir Thomas Lewis in his recent book on "Pain" makes an interesting observation on the antrum. Briefly, the mucous membrane of the antrum was stimulated through the opening made by a radical operation. The stimulation was electrical; in about eight minutes a little smarting was felt in the region of the malar process and lower eyelid, gradually the whole face became hyperalgesic, a small part of the temple, the ala of the nose and the skin of the upper lip. The same result was obtained if the nerves to the teeth were stimulated. A just perceptible flush appeared too. An exactly similar area of hyper-algesia was set up by catarrh of the antrum in this patient.

The fifth nerve is very apt to refer pain from the deep structures.

(a) Reference may be from one branch to another of the same division; the common example is the reference of pain from the lower teeth to the ear. It is stated that pain is never referred from one side to the other but I have seen one case in which pain from a right lower carious premolar was felt in the left ear so severe as to keep the girl awake for two nights; extraction of the tooth immediately relieved the pain. Incidentally, most of us must have been annoyed to find how difficult it is to decide whether pain is in the suspected lower molar or its opposite number in the upper jaw.

(b) Reference from a branch of one division to a branch of another division. This is the more common. Teeth again supply examples; a carious lower canine sometimes gives rise to supra-orbital pain. I have seen one case in which a carious lower molar not only gave rise to earache but also to pain behind the eye; extraction relieved both. I felt that the eye pain must have been due to reference along the orbital branch of the second division supplying the periosteum of the orbit.

The commonest example is supra-orbital pain from antral infection; another cause of referred supra-orbital pain is less recognized or at any rate seldom mentioned, that due to acute tonsillitis or pharyngitis; not only is pain experienced along the course of the nerve but hyperæsthesia too.

Pain due to affection of the sphenoidal sinus is frequently referred to remote parts of the head, e.g. to the occipital area, behind the ear and the top of the head; apparently the nerves involved are the meningeal branches from the Gasserian ganglion; the occipital pain must be felt *via* the tentorial nerve; the post-aural *via* the branches that pass from the ganglion backwards to enter the petrous bone and supply the mastoid antrum and cells. On one occasion I saw a doctor who complained of pain behind and above the ear; owing to the previous removal of the middle turbinal the *ostium of the sphenoidal sinus* was easily visible; on touching with a probe the lower edge of the ostium he pointed to a small spot behind and above the pinna where he felt pain.

On another occasion I saw a case of acute sphenoidal sinus suppuration in which the pain over the mastoid was so severe that mastoiditis was suspected, and on account of very high temperature and rigors, lateral sinus thrombosis too. The local signs were so slight that referred pain was suspected; exploration of the sphenoidal sinus revealed pus and drainage relieved the symptoms and cured the patient.

Since the Gasserian ganglion appears to supply sensation to the deep tissues as well as to the skin, removal might be thought to prevent all pain over that side of the head. However, Lewis mentions that it has been suggested that pain paths from the deep tissues may not arise from the ganglion; that parts of the face appear sometimes to respond painfully to deep pressure though the skin was rendered insensitive by division of the sensory branch of the fifth nerve; but H. M. Davies failed to find evidence of deep pain sense in cases in which the Gasserian ganglion had been removed. Recently I have seen a case which supports the first contention; the ganglion had been removed on account of trigeminal neuralgia involving the first and second divisions; the neuralgia had started after a radical antrum operation and later an external fronto-ethmoidal had been performed. After removal of the ganglion the patient had been free from pain for two to three years; she then began to have pain in the area of the fronto-ethmoidal scar which was tender; the wound was opened and pus found and the pain relieved. The skin of the whole of that side of the face and forehead was insensitive to touch.

From experience in a number of cases of migraine I am convinced that removal of the anterior end of the middle turbinal cures certain cases of supra-orbital pain indistinguishable from migraine in position and character, irrespective of whether Sluder's suggested *vacuum* theory is correct.

The ninth nerve appears to be even more apt to refer pain remotely; the statement that a lump in the neck and a piece of wool in the ear is diagnostic of growth in the deep pharynx is as true as any sweeping generality. It is at any rate true that pain in the ear (without local change) may be the only indication of a carcinoma of the aryepiglottic fold. The pain in the ear so common after tonsil removal is a typical example of referred pain along the ninth nerve.

In the œsophagus: the pain of a growth or impacted foreign body is often referred, either to the suprasternal notch or epigastrium even though the lesion is in the middle of the tube.

Wilfred Harris: The three sensory cranial nerves that may be associated with pain are: (1) The geniculate branches of the seventh nerve, derived from the pars intermedia Wrisbergi; (2) the fifth or trigeminal nerve; and (3) the ninth or glossopharyngeal nerve.

Geniculate zoster may be extremely painful, the pain being accompanied by the typical herpetic rash on the posterior wall of the auditory meatus, and even on the tympanum, in the cleft between the pinna and the scalp, and inside the mouth, along the side of the tongue and on one side of the hard palate. This distribution of the zoster rash is likely to be accompanied by loss of taste on that side of the tongue and palate. I well remember the first case I saw many years ago, which was referred to me by Dr. William Hill, whom some here may remember. He was puzzled by the blood-stained discharge from the ear, accompanied by considerable pain, that was complained of by another St. Mary's man, an Infirmary Superintendent in the country. Dr. Hill syringed out the ear, with a resultant excessive increase of the pain, which lasted for several weeks. In some cases facial paralysis accompanies geniculate zoster, indeed it is surprising that it does not always do so, when we recall the intimate relationship of the motor seventh nerve to the geniculate ganglion, which may be looked on as the posterior root ganglion of the facial nerve, and comparable to a spinal root ganglion. Very rarely persistent otalgia or geniculate neuralgia may be a sequel of zoster, or even of chill to the ear without an herpetic rash.

Glossopharyngeal tic douloureux is a rare but violently painful affection, exactly comparable in character and severity with trigeminal tic, though its frequency is perhaps not more than 1 to 500 cases of the latter. The pain may be spontaneous, or evoked by the act of swallowing, or by touching the tonsil, and is referred to the throat and ear, the latter probably through the nerve of Jacobson, and just in front of the ear at the back of the mandible, never to the chin, lip or tongue or side of nose, as in trigeminal tic. The spasms are brief, and are often accompanied by a hawking cough, as if to clear the throat, an attempt by the patient to mitigate the pain. It may rarely be bilateral, and may even be present with trigeminal tic in the same patient. A cure

may be effected by avulsion of the glossopharyngeal nerve from the jugular foramen after careful dissection, or by dividing the nerve intracranially. I have seen severe bouts of pain produced in the throat, associated with intense hyperæsthesia of the skin below the ear, in a case of a small recurrent carcinoma of the tonsil, ten years after a primary extirpation by the late Sir Charters Symonds. I took the case to him, and at first he could not believe there was a recurrence, but he excised the small growth, the size of a split pea, with relief of the pain, though a few months later further pain in the neck with numerous cutaneous metastases occurred.

Superior laryngeal neuralgia I have seen only a few times, once apparently spontaneous, but the common cause is tuberculosis of the epiglottis and larynx.

The fifth cranial or trigeminal nerve is responsible for the large majority of neuralgias about the face, jaws and sinuses. *Antral* infections and abscess cause local pain in the cheek, with tenderness, and with an acute abscess the pain reference may spread to the other two main trigeminal branches on the same side, involving the whole territory of the fifth. The pain may spread into the neck and down the arm even to the fingers. The same may be seen in dental neuralgia occasionally, especially with a carious lower molar, pain deep in the ear being a common reference. This no doubt is produced through the branch of the auriculotemporal nerve, itself one of the three main divisions of the mandibular nerve. This branch supplies the anterior wall of the external auditory meatus and the tympanum too in part, so that when this nerve is anæsthetized, as in alcoholic injection of the foramen ovale, the tympanum may be touched without producing the intense sensitiveness that is the normal condition.

It is well known that chronic antral abscess, instead of local pain in the face, may cause recurrent headaches, which I have known last for three years before their cause was discovered.

Frontal sinusitis is likely to be associated with pain referred along the supra-orbital nerve, with tenderness at the notch. External operations on this sinus, besides causing unsightly scarring, may be followed by persistent supra-orbital pain and hyperæsthesia, varying in severity. This pain is rarely relieved by alcohol injection at the notch, and this is a method I now never use. I have recently had under my care a New Zealand doctor who had suffered severely for over twenty years, and had had numerous operations, 38 in all, on the sinuses, including both frontals. To cure his pain it was necessary to inject the inner portions of both Gasserian ganglia, so as to get permanent anæsthesia of the forehead and cheeks. Though this appears, and is, a drastic treatment, involving permanent anæsthesia of both corneæ, it relieved his pain completely, so that he could sleep in comfort for the first time in twenty years.

Migrainous neuralgia is a name I use for a not uncommon form of pain around the eye and upper cheek and temple, often limited strictly to one side, lasting for a day or two days, sometimes only for an hour or two, or even for as short as ten minutes, so that six or more attacks may occur daily. Unlike ordinary migraine it is never preceded or accompanied by visual spectra, and very rarely by vomiting, though sometimes with nausea. In some patients the common type of migraine in adolescent life changes in the middle twenties or later to migrainous neuralgia. It is really a dural headache, and responds instantly to alcohol injection of the inner half of the Gasserian ganglion. Although occasionally alternating from one side to the other in different bouts of the headache, which may recur daily for three to six weeks, sometimes annually, very often the pain is strictly limited to one side. This is more suitable for alcohol injection. Peripheral supra-orbital injection is usually quite useless, though I have known infra-orbital injection give complete relief for five years. The majority of these sufferers have been seen by ophthalmic surgeons, and glasses prescribed, and in many, operations such as turbinectomies, antral washouts, even up to exenteration of the ethmoid and antra, have been done without relief. Some have been labelled as cases of Sluder's neuralgia, and treatment by cocainization or alcohol injection of Meckel's ganglion performed. It is possible that sphenoidal sinusitis may account for a few cases of so-called Meckel's neuralgia, as the great superficial petrosal nerve which runs from the geniculate ganglion to Meckel's is in close relationship to the sphenoidal sinus in part of its course.

Chronic neuralgia of the jaws is another troublesome type of facial neuralgia. This affects sometimes the upper, sometimes the lower jaw, and is occasionally bilateral. The pain is often described as "drawing" and burning, with some shoots of pain, varying in severity, but more or less constant. The Americans class it as "Atypical Neuralgia", because it differs from true trigeminal tic. The pain may appear to start in one tooth, and spread along the jaw as teeth are extracted. In a number of cases the pain com-

mences after wholesale dental extractions, in my opinion always a dangerous neurological shock. The constancy of the pain, its burning and drawing character, are suggestive of its type, and it is important to recognize it, as any operative procedure aggravates the pain. Alcohol injection in particular must be avoided, as the patient then has the numbness to complain of as well as the pain. A curious fact is that a small proportion of cases of true trigeminal tic may develop this type of pain some weeks after Gasserian injection or root resection. I call it *trigeminal causalgia*, and it is very difficult to relieve. Undoubtedly this type is particularly likely to be met with in neurotic subjects, and we must be wary of producing extensive and permanent anæsthesia in such subjects.

Trigeminal zoster, usually involving the ophthalmic branch, is one of the most troublesome causes of persistent pain, and may lead to suicide.

Malignant growths of the jaws and tongue cause sometimes severe agony over long periods, especially the nasopharyngeal neoplasms which are liable to cause intense pain along the mandible and tongue, or upper jaw.

Growths in the maxilla or antrum, ulcerating through the hard palate, are very distressing cases, and cause severe persistent pain, but these can often be completely relieved of pain by Gasserian injection. Similarly recurrent carcinoma of the tongue and floor of the mouth may be completely relieved of pain by alcohol injection of the foramen ovale.

Spasmodic neuralgia of the face, simulating trigeminal tic somewhat closely, may be produced by *local lesions* of the teeth or even the cheek and facial bones, which may have escaped detection for many years (*see* Fagge's "Principles and Practice of Medicine", 1886, vol. 1, p. 359). Many dental cases of severe persistent and intermittent neuralgia may be due to caries of the necks of teeth obscured by the gum. I remember such a case which had been classed at one hospital as malignant disease and as tic douloureux at another, in which X-rays cleared up the diagnosis. Pulp stones and exostoses on the roots may also cause difficulty in diagnosis. A dentist who was asked to look after a gentleman who suffered violent intermittent pain in one lower jaw went over each tooth with meticulous care on two occasions, and on the second inspection he detected a tiny hole in the first molar at the gum level, and alternate hot and cold water syringing of the tooth gave a sharp reaction of pain. He persuaded his patient to allow him to extract the tooth, which on section disclosed a bristle of a toothbrush in the tiny hole, reaching well into the dentine. The neuralgia ceased at once after the extraction.

True trigeminal tic, or tic douloureux, is a disease which, once contracted, always recurs at shortening intervals for the rest of the sufferer's life, unless the trigeminal sensory root is divided, or the Gasserian ganglion destroyed by alcohol injection. Yet, in its early stages—before the pain develops its typical tic characters, with sudden violent spasms of pain, lasting a few seconds only, though perhaps recurring every two or three minutes—only too often are good teeth sacrificed one by one, or wholesale, in the vain effort to stop the neuralgia. So too antrotomies or intranasal operations may be suggested. Be wary therefore of sudden spasmodic facial neuralgias, especially if started by the movements of eating, washing the face, or by light touches on the lips, nose, or eyebrow.

C. P. Wilson discussed the varieties of pain to which a patient might refer as being behind the eye.

Pain due to irritation in the neighbourhood of the Gasserian ganglion was seen typically in cases of apical petrositis, and in this condition, although the patients complained of pain behind the eye, they usually pointed with their hands to the temporomalar region. The type of pain found in a typical attack of migraine, although described as being behind the eye, was more difficult to describe accurately or to locate, and one received the impression of a "block" pain around the orbital region, often with local tenderness. The hand might be pointed to the frontal region, but in general the whole orbit was covered. In many attacks of pain of a similar nature which were sometimes called atypical attacks of migraine, in that they were unassociated with visual symptoms, the patient referred the pain to the inner side of the orbit, sometimes the fronto-orbital region and sometimes the maxillo-orbital, but always to the inner side. He suggested that these cases might be associated with an œdema in the neighbourhood of the spheno-palatine ganglion. Certainly many of them had quite definite appearances of a vasomotor œdema affecting the nasal mucosa, and the majority exhibited other evidences of a poor vasomotor tone. In very severe attacks there might be an associated vasomotor

crisis, with lacrimation and profuse rhinorrhœa, and such attacks might be dignified with the description of sphenopalatine neuralgia. These cases seemed to be particularly common at the present time, and usually showed some thickening of the lining membrane of the antra, although not usually of the frontal sinuses. They were most common in women, and were generally associated with a low blood-pressure. Aspiration of the sinuses sometimes produced a little mucus, but if this were examined it was found to be mucus and not mucopus, although eosinophil cells were commonly seen. This type of pain was often relieved by cocainizing the region of the sphenopalatine ganglion locally. It was sometimes relieved by the local use of ephedrine or adrenaline, but this was not necessarily due to a local effect as improvement occasionally occurred on spraying the opposite side of the nose with adrenaline. Such cases had to be diagnosed from attacks of sphenoidal sinusitis: blocking of the sphenoidal ostium with rejection of radio-opaque fluids was a feature of the attacks, and did not imply that sinusitis was present.

Another cause of a similar type of pain which he had been disinclined to recognize for some time was that associated with an enlargement of the shell of one middle turbinate, due to distension of the included ethmoidal cells. Such cases occurred between the ages of 18 and 25, which was the age at which simple developmental deformities of the nasal septum reached their peak. The only treatment necessary was to crush the shell of the turbinate with a pair of ethmoidal forceps, and there was no need to remove any part of the turbinate.

He also mentioned briefly the referred earache associated with the glossopharyngeal nerve, and commented upon the fact that occasionally patients with an intrinsic carcinoma of the larynx did get an earache on the same side, even without associated perichondritis, or obvious spread to the pharyngeal wall. It was difficult to understand the mechanism of this, unless the glossopharyngeal nerve sent some fibres down the aryepiglottic fold to communicate with branches of the internal laryngeal nerve.

He agreed with Mr. Mollison's observations concerning the difficulty experienced in locating pain, and illustrated the case of a patient with an ossified stylohyoid ligament which was pressing on the capsule of the tonsil. The patient had had all six molar teeth removed on that side at different times within the year, having associated the pain which she was getting with the teeth. Removal of the lower one inch of the ossified ligament had completely cured the pain, although she had quite severe earache for a few days after the operation.

Captain J. G. Schoolman, U.S.A.M.C., spoke of the variety of head pains of mechanical origin which might be distributed not only to the ear but to the sinus region, and to the neck, and might give every type of pain picture. Fluoroscopic motion pictures taken of the head during the mastication of food showed how the number and condition of the teeth and temporo-mandibular joint pathology might affect mastication and give rise to referred pains.

Major E. P. Fowler, Jr., U.S.A.M.C., said that with regard to the deep pain behind the eye in petrositis, the petrosal nerve appealed to him as a possible cause rather than the fifth nerve. This nerve went through a very narrow bony foramen and it was very much easier to get an infection that involved this nerve, because in very few temporal bones did infected air cells go as far forward as the Gasserian ganglion.

E. D. D. Davis said that neuralgia of the alveolus after extraction of teeth in neuropathic women could be very intractable; all kinds of treatment had failed. Incision of the alveolar gum and removal of bone, blocking of the infra-orbital nerve and even washing out of the antrum might relieve the pain for a short time. The cause of the neuralgia was unknown but it might be a localized periostitis.

R. J. Cann said that he had rather hoped that Captain Weddell might clear up the mystery why pain never arose from the glossopharyngeal nerve in the throat as a result of a lesion in the ear. Why should there be this one-way traffic? A patient came to him complaining, with a certain hesitancy, that he had a pain in the tip of his nose which kept him awake at night. On examination he found nothing wrong with the nose at all, but the attention of the dentist was needed. The dentist discovered that the man had a small dental cyst at the apex of the central incisor and the removal of that cyst cured

mences after wholesale dental extractions, in my opinion always a dangerous neurological shock. The constancy of the pain, its burning and drawing character, are suggestive of its type, and it is important to recognize it, as any operative procedure aggravates the pain. Alcohol injection in particular must be avoided, as the patient then has the numbness to complain of as well as the pain. A curious fact is that a small proportion of cases of true trigeminal tic may develop this type of pain some weeks after Gasserian injection or root resection. I call it *trigeminal causalgia*, and it is very difficult to relieve. Undoubtedly this type is particularly likely to be met with in neurotic subjects, and we must be wary of producing extensive and permanent anæsthesia in such subjects.

Trigeminal zoster, usually involving the ophthalmic branch, is one of the most troublesome causes of persistent pain, and may lead to suicide.

Malignant growths of the jaws and tongue cause sometimes severe agony over long periods, especially the nasopharyngeal neoplasms which are liable to cause intense pain along the mandible and tongue, or upper jaw.

Growths in the maxilla or antrum, ulcerating through the hard palate, are very distressing cases, and cause severe persistent pain, but these can often be completely relieved of pain by Gasserian injection. Similarly recurrent carcinoma of the tongue and floor of the mouth may be completely relieved of pain by alcohol injection of the foramen ovale.

Spasmodic neuralgia of the face, simulating trigeminal tic somewhat closely, may be produced by *local lesions* of the teeth or even the check and facial bones, which may have escaped detection for many years (*see* Fagge's "Principles and Practice of Medicine", 1886, vol. 1, p. 359). Many dental cases of severe persistent and intermittent neuralgia may be due to caries of the necks of teeth obscured by the gum. I remember such a case which had been classed at one hospital as malignant disease and as tic douloureux at another, in which X-rays cleared up the diagnosis. Pulp stones and exostoses on the roots may also cause difficulty in diagnosis. A dentist who was asked to look after a gentleman who suffered violent intermittent pain in one lower jaw went over each tooth with meticulous care on two occasions, and on the second inspection he detected a tiny hole in the first molar at the gum level, and alternate hot and cold water syringing of the tooth gave a sharp reaction of pain. He persuaded his patient to allow him to extract the tooth, which on section disclosed a bristle of a toothbrush in the tiny hole, reaching well into the dentine. The neuralgia ceased at once after the extraction.

True trigeminal tic, or tic douloureux, is a disease which, once contracted, always recurs at shortening intervals for the rest of the sufferer's life, unless the trigeminal sensory root is divided, or the Gasserian ganglion destroyed by alcohol injection. Yet, in its early stages—before the pain develops its typical tic characters, with sudden violent spasms of pain, lasting a few seconds only, though perhaps recurring every two or three minutes—only too often are good teeth sacrificed one by one, or wholesale, in the vain effort to stop the neuralgia. So too antrotomies or intranasal operations may be suggested. Be wary therefore of sudden spasmodic facial neuralgias, especially if started by the movements of eating, washing the face, or by light touches on the lips, nose, or eyebrow.

C. P. Wilson discussed the varieties of pain to which a patient might refer as being behind the eye.

Pain due to irritation in the neighbourhood of the Gasserian ganglion was seen typically in cases of apical petrositis, and in this condition, although the patients complained of pain behind the eye, they usually pointed with their hands to the temporomalar region. The type of pain found in a typical attack of migraine, although described as being behind the eye, was more difficult to describe accurately or to locate, and one received the impression of a "block" pain around the orbital region, often with local tenderness. The hand might be pointed to the frontal region, but in general the whole orbit was covered. In many attacks of pain of a similar nature which were sometimes called atypical attacks of migraine, in that they were unassociated with visual symptoms, the patient referred the pain to the inner side of the orbit, sometimes the fronto-orbital region and sometimes the maxillo-orbital, but always to the inner side. He suggested that these cases might be associated with an œdema in the neighbourhood of the spheno-palatine ganglion. Certainly many of them had quite definite appearances of a vasomotor œdema affecting the nasal mucosa, and the majority exhibited other evidences of a poor vasomotor tone. In very severe attacks there might be an associated vasomotor

Section of Radiology

President—N. S. FINZI, M.B.

[*November* 19, 1943]

DISCUSSION ON THE ORGANIZATION OF A FLUOROGRAPHIC SERVICE FOR THE CIVILIAN COMMUNITY

Dr. Maurice Davidson : The practical difficulties of mass radiography by the ordinary method, using large films of standard size, are obvious, but they have been surmounted by the introduction of special apparatus designed to take radiographs on miniature films which can then be projected on to a screen and enlarged to a size sufficient to permit of the recognition of doubtful shadows or obvious abnormalities. It must be emphasized that diagnosis must not be made at this stage. The main object of this method is to enable large numbers of individuals to be examined in a relatively short time; those who are found suspect are referred for complete examination by standard radiography and also, if necessary, by clinical and bacteriological methods.

With the technique of miniature radiography I am not immediately concerned, except to insist that the best and most efficient apparatus is essential, and that the subsequent study of the projected films must be carried out by radiological and clinical experts working in conjunction. I should add that, owing to the fatigue element, there must be a definite limit to the number of films which they can be asked to read and to the length of time they can be expected to work at a sitting. My primary object at this meeting is to insist on the importance of this work to social medicine, and to urge the universal adoption of mass radiography as a real and necessary contribution to the problems of preventive medicine, and especially to the prevention of tuberculosis.

Reviews of large numbers of radiographs taken from apparently healthy individuals have shown a small but fairly constant percentage of pathological lesions. These include various conditions, the most important of which is tuberculosis, and it is to this that I propose in the main to invite your attention. As you know, investigations in this direction have so far been carried out chiefly in H.M. Forces, in which the difficulties which we shall have to consider in organizing a fluorographic service for the civilian community do not obtain to the same degree. The figures already published are, doubtless, well known to most of you, and I need only remind you briefly of some of the salient points.

In Surgeon Rear-Admiral Dudley's series (18,751 cases) 0·25% of the total were found to have active lesions. In Cooper's series (22,000 cases) the percentage was 0·49, and in Galbraith's (100,000 cases) it was 0·56. Other observers, working on the same lines, have obtained similar results. The percentages of cases of active tuberculosis discovered, which do not seem to vary greatly, may at first sight appear small, but if we consider what they indicate when applied, as is presumably intended, to many millions of the civilian population, the absolute numbers of cases of active pulmonary tuberculosis which we may expect to find among the apparently healthy will doubtless come as a considerable shock. It is, I suppose, this fact more than any other that must bring home to those who advocate the introduction of this method into our public health system the difficulties likely to be raised thereby. It is of paramount importance that these should be clearly recognized in order that they may be squarely faced and overcome. As in other problems which concern the health of the community, the attitude adopted by the governing authorities is likely to be conditioned to a large extent by the opinions held by the Medical Profession, and by the determination or otherwise with which those of us who are in a position to do so are prepared not only to maintain but also to promulgate their views.

Despite the enormous amount of work that has been published in the last few years on the early lesions of pulmonary tuberculosis there are still far too many clinicians who fail to understand that the spreading granuloma may be, and in fact very often is, entirely symptomless. It seems to me desirable to mention this point here, since it is, perhaps, not the least among the difficulties with which we may have to contend in our efforts to organize a fluoroscopic service. In view of the neglect of X-ray diagnosis of which some practitioners are still occasionally guilty, even in the case of patients whose departure from the normal standard of health is admitted, I feel that further education of the clinician in regard to the silent pulmonary lesion in tuberculosis is

him instantly of the pain in the tip of his nose. A curious instance which one met occasionally was a disturbance of taste after a tonsil operation. Several patients complained bitterly for many months of the taste of iron or something rather bitter and unpleasant every time they ate.

Wilfred Harris, in reply, said that in his experience the complaint of pain in or behind the eye was a very constant one. It usually disappeared after injection of the Gasserian ganglion. But there were cases in which the pain was complained of all around the eye, and which did not disappear under any treatment. He thought that "psychalgia" was the proper name for such conditions. After all, the eye was the part of the body which one regarded as most closely identified with oneself, and if there was referred pain as in psychalgia it was liable to be referred to the eye rather than anywhere else. He had seen a case of apical abscess of the central incisor, but the pain was referred up the side of the nose. When the tooth was removed the referred pain disappeared.

Pain in the ear was commonly connected with the glossopharyngeal nerve, and spasmodic pain occurring in the ear was strongly suggestive of that origin. He presumed that it might be referred through Jacobson's nerve. He could not explain the "one-way traffic". The "ice-cream complex" was very common. It referred to the side of the head after eating anything that was very cold. The reference was presumably up the vagus nerve and thence to the fifth nerve, and so to the various areas supplied by the fifth.

abnormal shadows found. I suggest that such control should be at monthly intervals for a period of three months: then, if the appearances are stationary, at two-monthly intervals for six months; then at three-monthly intervals for twelve months; after this, at longer intervals, say every two years.

The problem of compensation which may have to be faced is one of even greater magnitude. The financial liability involved therein may well prove to be monumental.

I am not at this moment prepared to offer any concrete solution of these difficulties, indeed I doubt whether the questions that I have raised can be adequately answered at this stage of our inquiry. I have felt, however, that the main object of my remarks, which are intended only to be introductory, should be to raise these points, and I hope that other speakers whose work is more especially concerned with the administrative side of public health may be able to throw further light on them and to indicate the lines on which a satisfactory approach to this problem can best be started.

Dr. Peter Kerley: The three main points for discussion are the equipment, the constitution of the team and the arrangements for the disposal of the pathological cases.

The equipment has been described in detail in various technical journals and consists of a 400 ma. four-valve unit energizing a rotating anode tube. The camera is automatic with a 1·5 coated lens. Eventually each unit will have its own mobile generator.

The unit is fairly easily transportable and turns out both large and miniature radiographs of the highest quality. The technique has been standardized according to the thickness of the subject on a series of 20,000 people of different age-groups.

The key people in the team are the Medical Director, the Senior Radiographer and the Organizing Secretary. The last two can relieve the Medical Director of everything except purely medical work. An experienced team can easily handle 1,500 cases a week.

Miniature films can be read accurately at a rate of 400 per hour. This figure has been obtained by checking different observers on the same batch of films. Reading of miniatures is only a question of spotting obvious deviations from the normal. Reading large films is a problem in differential diagnosis, requiring considerable experience. Ability to read miniatures rapidly and accurately is probably determined by visual memory. Reading large films should only be carried out by experienced medical men and it is hoped that interpretation of these will always be carried out jointly by a physician and a radiologist.

The tuberculosis cases detected fall into four groups: (*a*) The obvious chronic cases with extensive fibrosis and cavitation. (*b*) Acute cases with cavitation in young adults. (*c*) Old cases with extensive calcification and fibrosis, but showing nodules the age of which cannot be detected by radiography. (*d*) Minimal lesions in young people with no physical signs or symptoms and no certain criteria on which the prognosis can be evaluated. These are referred to as latent subclinical tuberculosis and offer the greatest problem in their disposal. Antero-posterior as well as postero-anterior views have proved invaluable in determining whether the type of lesion is old or recent and the taking of pictures in these two positions is advised in all doubtful cases (figs. 1 and 2).
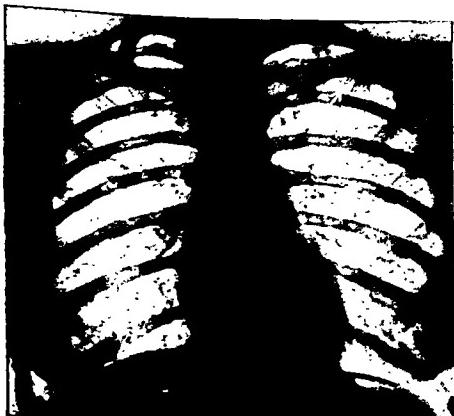
FIG. 1.—Routine postero-anterior view, showing top focus behind the left clavicle. (Large film.)
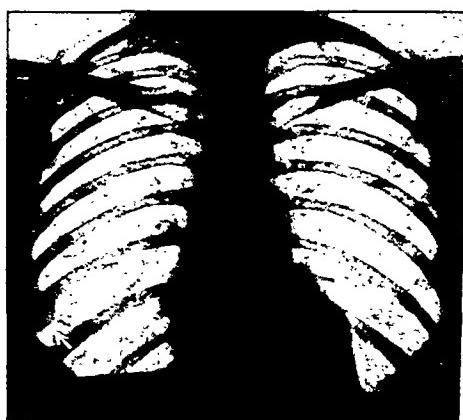
FIG. 2.—Antero-posterior view of fig. 1, showing discrete foci in left upper lobe and round focus, cavitating, in the periphery of the right lower lobe. (Large film.)

still an urgent need and that I need make no apology for reiterating what to most experts in this branch of medical diagnosis is now almost a platitude. The pioneer work that has been carried out on the investigation of child contacts, with all the trenchant evidence afforded by serial radiographs, should be sufficient to convince the most ignorant or sceptical. There is, however, still more prejudice on this point, and I allude to it first as a difficulty which still has to be dealt with and which, since it originates in our own ranks, we and we alone can overcome. To do so is our primary duty.

We have now to consider a problem of a rather different character, namely that of how to deal with the administrative difficulties associated with the civilian service we advocate and the various matters of policy and professional ethics which will inevitably arise from its introduction on a universal scale. The education of the practitioner and the task of persuading him to adopt a new, and in the eyes of many a revolutionary, method of diagnosis is, from our point of view, a purely domestic affair. When we come to the wider implications of a national fluorographic service we are faced with questions which will demand no little tact and diplomacy. The application of a system of examination to large numbers of civilians in peacetime can hardly be attained with the ease that is possible in the Services, in which a considerable amount of regimentation is regarded as the natural order of things. In the ordinary life of the civilian community the position is different, and the problem is one which, from the point of view of the governing authorities, will have to be handled in a totally different manner. It is obvious that the enlistment of a large number of citizens as participants in a scheme which involves their submission to any form of medical examination must be voluntary, and the success of the scheme will be proportionate to the extent to which the examinees are willing to co-operate from the conviction that it is in their best interest so to do. It may at first sight appear that such co-operation is not hard to obtain, and indeed the attempts already made, so far on a comparatively small scale and in selected sections of the population, have given promise of a fair degree of success. When, however, the system is applied to really large numbers of the industrial population the difficulty is likely to be greater, and the utmost care will have to be exercised lest the spirit of co-operation inherent in a majority becomes infected, as may easily happen, by the unreasonable prejudice of those few recalcitrants who are always ready to throw discredit on any scheme that involves the slightest demand upon their personal convenience. Even if the initial difficulty is surmounted, we have still to envisage the position of the medical experts who, as a result of a radiological examination of all the workers in a large industrial concern, find themselves in possession of the knowledge that a number of the employees (let us suppose for the sake of argument 50 individuals, i.e. 1% of a total of 5,000) have pulmonary lesions which are potentially dangerous and which therefore demand further investigation. Of these 50 individuals perhaps one-half (i.e. 0·5% of the total examinees) may then be found to have active tuberculosis.

Now this knowledge is, of course, a matter of professional confidence. It cannot without the full consent of the individuals concerned be divulged to anyone: I presume that even the patient's own private doctor cannot be excepted, and certainly not the employer. How then shall we stand in the matter? The position is not fundamentally different from that of a patient who comes to hospital because he complains of symptoms and is then found to be suffering from phthisis, though in that case the shock of the diagnosis is possibly somewhat less, since anticipation of the verdict is perhaps to some extent inherent in his decision to seek the doctor's opinion. When, however, the bomb-shell has been dropped on him as a result of an unfamiliar method of examination to which he has been persuaded to submit himself by an enthusiastic scientific experimenter (for so the mass radiologists may well be regarded by quite a number of the examinees, whatever explanation of the procedure is vouchsafed to them) the resulting psychological reaction is likely in many cases to be somewhat more serious. The possible repercussions of such a reaction form one of the problems with which we shall have to deal and which, at this early stage of our efforts, I think it is prudent to anticipate.

There remain for consideration such questions as the provision of facilities not only for the complete examination of suspects, but also for the treatment of those for whom treatment may be necessary, the problem of compensation for employees who are found temporarily or permanently unfit to continue their work in the job which they held at the time of their examination, and the provision of allowances for their dependants. The introduction of mass fluorography on a really large scale will lead to the discovery of certain numbers of cases of active tuberculosis that will need immediate treatment in hospital, in sanatorium, or elsewhere. There will also be those who require complete investigation to establish a diagnosis. A third group, and this is of the utmost importance, will require X-ray control *over a period of years* to watch any changes in the

While Service units must differ from civilian units in that their immediate aim is an answer on fitness for acceptance into, or continuance in the various duties of the fighting forces, they do not differ at the extremes of diagnosis and disposal. The method is new enough not to have acquired any of the rules and criteria that must of necessity be employed for certain Service purposes, while disposal must be a civilian problem in that the fighting forces of to-day are to some nine-tenths of their strength civilians in uniform.

Service and civilian units differ in the comparative ease with which numbers of disciplined examinees can be found. Much wise propaganda and personal contact with bodies of the population will therefore be necessary. It appears, however, that the scheme has the backing of many of the trades union officials throughout the country, and the film prepared by the National Association for the Prevention of Tuberculosis will be of decided help.

Necessities for efficient organization can be summed up under the headings of "External" and "Internal".

On the "external" we may have general agreement. Thus, we know that among each 1,000 of the supposedly healthy we are likely to find some 4 who will require observation or treatment for pulmonary tuberculosis. No unit should commence work until it has priority call on a number of beds appropriate to its programme for the first year; thus, if preliminary contacts in the district promise 10,000 examinees, 40 sanatorium admissions must be available over that year. This means some 30 beds occupied by the end of the year, for while most active cases are likely to be found before the stage of disease requires hospitalization, and the majority will need an average of four to six months' treatment, some will require short period observation, some will be advanced, and some will require collapse therapy from pneumothorax to thoracoplasty. To this proposal · there will be the objection that there is already a waiting list for sanatoria. The answer must be that the failure to provide immediate treatment will inevitably repercuss on the unit; if we are not to invite failure we must perforce take the long view, even if we appear thereby to be unfair to the patient diagnosed at other clinical centres, private or public.

The same argument must apply to the discovery of cases of non-tuberculous lung disease and heart disease. Definite and preliminary arrangements must be made with a chest centre in a general or special hospital to take cases for out-patient and in-patient investigation and treatment. "Follow up" alone will be greatly facilitated by such a plan; it will avoid what should be a totally unnecessary worry to the unit administration in its attempt to keep efficient records on ultimate diagnosis and disposal.

Under this heading we may consider also the specialized training of the non-medical members of the unit teams, and the acceptance by the appointed medical officers of some basic criteria on medical control and on the methods of recording all findings, radiological and clinical. Thus, uniform methods of positioning, assessment of kV. and ma. and processing of films are essential if the required high standard on the one hand, and comparability of results on the other are to be attained.

Central teaching seems therefore to be the ideal. Without it we are certain to do injustice to the examinee, in whom it is as dangerous to find non-existent disease as it is to miss an early lesion, particularly if this be due to failure to take full advantage, through avoidable personal error, of the capacities of the X-ray machine. The same applies to interpretation. Difficult though it must be to get total agreement, some common fundamentals on the reading and recording, objective and interpretive, of abnormal shadows should be detailed at a central unit if we are to avoid the criticism that the method is much more spectacular than useful.

On the "internal" side, that is, on the details of the working of the unit, there may be marked differences of opinion. Everyone who has had charge of a unit must be biased, not only by his individual experience in that unit, but by his preceding training, clinical and radiological, which is bound to colour his approach to diagnosis and therefore his ideas on the powers and limitations of the medical man in charge. The following ideas may appear dogmatic; they are nevertheless the result of much thought on fairly extensive experience from fully 300,000 examinations in six mass X-ray units.

The medical man appointed must be the best available, experienced enough to command respect but young enough in mind, if not in years, to learn as well as to apply his knowledge. Once appointed, he should be trusted completely, remain in charge wherever the unit goes, and not be hedged about by irritating limitations. This is as true of good medical as it is of good business decentralization. He should not be the overseer of an "automatic machine", merely sifting normal from abnormal miniatures. No self-respecting medical man would take on or remain at such a post. Only by being empowered to follow up his abnormals on the lines of a well-run out-patient department of a chest hospital or dispensary can he hope to keep alive mentally. The clinical

Experiments show that first-stage silicosis can be detected on miniature films. Cardio-vascular cases are also easily detected and it is recommended that for the present no action can be taken on these except in young people. In most instances so far, young people with valvular and congenital diseases have been found to be aware of their disability.

The rounded pulmonary tumours are found fairly frequently; recommendation for treatment of these cases is difficult as there is no agreement on their prognosis. Some surgeons believe all rounded tumours become malignant while many physicians hold the opposite view. Until accurate data are compiled each case must be judged on its merits.

Dr. P. D'Arcy Hart: My experience is derived from the mass radiography survey in progress under the Medical Research Council amongst factory and office populations, the number covered being expected to reach about 20,000.

Approach to factory or similar group.—Although working people in general favour mass radiography, propaganda is required in individual units. This should stress that the scheme is voluntary and free, and that the results are confidential so that there need be no fear of victimization; explain the procedure of recalls for large films and for the medical interview; point out the necessity for 100% response, including previously diagnosed tuberculous cases; warn that the finding of a normal chest at one moment offers no guarantee for the future; and discuss the curability of tuberculosis in relation to its early diagnosis. The best means of carrying out the propaganda is through the shop stewards into the shops, i.e. using the workers' own initiative, and through individual leaflets in pay packets. From the management should be secured agreement on the confidential nature of the results, on granting of pay during the examination, and, where possible, the promise of a suitable job if and when the patient is fit to return to work. The best medium for discussion of the scheme in an industrial unit is a joint works council, factory health committee, or equivalent; failing this, the management and shop stewards' committee should both be seen.

Medical staff.—A medical director is necessary to give general direction to the team, to answer strictly medical questions arising in the arrangements of a survey in individual factories or other units, to interview abnormal tuberculous or non-tuberculous cases before disposal, and to analyse the results of the surveys. The main arrangement of the survey can be done by a lay liaison-officer or by the radiographer. The medical director may or may not be required to read the miniature films; he should certainly examine the large films, preferably with a radiologist. The director may be full-time, or he may be part-time, doing dispensary work in the rest of his time.

Disposal of cases.—Tuberculous cases can conveniently, from the administrative point of view, be classed into (*a*) previously diagnosed pulmonary tuberculosis; (*b*) persons with newly discovered T.B. lung lesions requiring medical action. The latter group can be sub-divided as follows: (i) requiring sanatorium or equivalent, (ii) requiring medical observation while remaining at work (which may be full or restricted), (iii) requiring a single precautionary recheck. The cases are best sent to the tuberculosis officer directly or through the general practitioner. Notification should be left to the doctor who will be responsible for the patient's care.

Future problems.—When the National Scheme is expanding, decisions will have to be made as to which are the susceptible groups requiring first attention; at what intervals radiography should be repeated; whether the survey should be restricted to local author-ities or whether large individual units or groups should be encouraged to have their own permanent apparatus; how far mass radiography should be combined, in young adults and adolescents, with tuberculin testing. The expansion of the scheme must be combined with rational education on the nature of tuberculosis. In my opinion the examinations under the National Scheme must remain voluntary, at least for the present; and no com-pulsion should be put upon the few persons who, mainly for economic reasons, are un-willing to leave work until safe and permanent employment can be offered to all persons with tuberculosis who are fit to work, whether they be infective or not. Such provision is as much a national responsibility as is mass radiography, and without it the latter cannot fully succeed.

Wing-Commander R. R. Trail: The responsibilities and implications inherent in the setting up of civilian mass radiography units must be realized, and the necessary arrange-ments resulting from them must be complete before the units commence work. Any other method of approach will mean confusion, and confusion will bring disrepute on this aid to diagnosis, which has already shown its value in its application to Service personnel.

of all examined since October 4, the diagnosis was probably tuberculous; in 0·23%, cardio-vascular and probably non-tuberculous lesions for investigation; in another 0·23%, further X-ray examination needed in a few months; in 1%, calcified lesions and no further immediate action necessary. This 1%, however, in the miniature films compares with 6·9% of calcified lesions found in large films taken in the course of routine examinations of student nurses.

The publicity work in the factories was done by the Borough Medical Officers of Health, and six to eight weeks' notice was essential. All those attending for examination came by appointment. It was important to warn them beforehand not to be alarmed if they were recalled for a large film to be taken. It was also emphasized that the result of the examination is confidential and no report on individuals would be made to the employer without the consent of the patient. A letter was not sent, even to the patient's own doctor, without his consent, but by only one patient so far had that been withheld.

The staff consisted of one medical officer, at present wholetime, two radiographers, one dark-room technician, one marshaller, two clerks with the unit and two at County Hall. There was a viewing panel to see the large films. The panel comprised chest physicians and radiologists. A day a week had to be set aside for taking large films and evening sessions might be necessary for this purpose. The proportion for whom large films were needed varied from group to group. Of the first 3,000 persons for whom small films were taken, 4% were recalled for a large film.

The numbers actually examined by mass radiography varied from 800 to 1,500 a week, but even 1,100 to 1,200 keep the staff very busy.

To save clerical work the patients were all told that they could regard the examination as satisfactory if nothing was heard within a fortnight. A letter was always sent to the patient if a large film had been taken. There were four stock letters—one to the effect that there was no evidence of disease and another that nothing of importance had been discovered (this applied to those with calcified lesions). The third asks the patient to attend again after an interval, which may be up to six months, for a further large X-ray photograph, and the fourth told him to go to his doctor. There was also a stock letter to the doctor, enclosing the films.

It was frequently necessary to provide transport from the factory to the place where the unit was located.

It was surprising how often the local electric supply cable was found to be inadequate and a special cable had to be put in. It would be a great advantage to have a mobile generator.

One difficulty had been that the bulbs for the projector were very short-lived and difficult to replace.

It was estimated that 100 extra sanatorium beds are needed for each set in active use.

Dr. Philip Ellman said that radiology through a well-organized and efficient mass fluorographic service for the civilian population had an opportunity of making a unique contribution to the social and preventive medicine of the future. Experimental work carried out by Clark, Cordiner and Ellman [1], working as a team in 1940 and 1941, had demonstrated the importance of close co-operation between technician, chest radio-logist and chest physician, for the proper staffing of a mass radiography unit for the civilian population. The films produced by the existing central unit set up by the Ministry of Health more than fulfilled these prerequisites but it seemed necessary for an assurance to be forthcoming that the multiple units that were to be sent out into the country should be consistently well staffed. The central unit had produced films which were in some cases, when projected, equal in detail to the full-sized film.

A great responsibility rested on the panel of examiners who were to interpret these miniature films with the speed and efficiency Dr. Kerley had mentioned. Dr. Ellman doubted whether anyone could be trained in a few weeks or months to take the responsi-bility of correct interpretation which was as great as, if not greater than, the interpre-tation of full-sized films. In his view the Ministry of Health might with advantage prepare a panel of examiners who would include an experienced chest radiologist and chest physician working closely together in order to avoid serious errors. Advances in all departments of radiology had been such that the opinion of the radiologist who had acquired special experience in chest diseases was naturally preferable to that of the more general radiologist without such experience. In this connexion Dr. Ellman agreed with Wing-Commander Trail that many tuberculosis physicians were, through specialized opportunities, in a better position to interpret chest radiographs, whether miniature or full-sized, than the average general radiologist. The same applied with equal force to cardiological interpretation. The necessary safeguard was, however, provided, when two individuals interpreted both miniature and full-sized films jointly.

side must keep pace with the radiological. Both sides will then benefit, his knowledge will increase steadily and, what eventually really matters, the patient will be the richer.

A Service unit can deal on these lines with 2,000 examinees per week. Miniature film is followed by large film and clinical examination. Out-patient observation is followed where necessary by in-patient observation. The civilian unit director will not have to keep up on an average more than half this number of examinations. He can, in the difficult case, have the opinion of the consulting radiologist and any necessary assistance from the local Tuberculosis Officer; with both he can maintain the closest contact. He will then be in the position to give an opinion on any abnormality found, to recommend what he considers the tuberculous case to the dispensary, the heart case to the appropriate physician, and the non-tuberculous lung case to the care of the specialist appointed, who will see it through to the necessary investigation and treatment, medical and surgical.

There are in the Public Health Services many keen Tuberculosis Officers who are chest physicians in the broadest sense, with a sound knowledge of modern methods of diagnosis and treatment. These men have the makings of ideal Unit Directors.

Dr. H. Jocelyn Smyly gave an account of his experience in chest fluoroscopy at Cheeloo University Hospital, Tsinan, North China.

Dr. L. Banszky said he did not agree with Dr. D'Arcy Hart that explanation to the workers is necessary before the radiographic examination of the chest is carried out. For the last seven years fluoroscopic examinations on employees had been carried out in one industrial firm, near London, and during this time not more than 10 people refused examination out of *circa* 20,000. The fluoroscopic test was part of the medical examination and was accepted as such by the majority of the workers.

When active tuberculosis was discovered in a case, X-rays, sputum tests and blood tests were carried out, and only when the diagnosis was established, was the patient notified that he was suffering from a lung disease. The patient was then sent up to a public hospital for a second opinion, and only when the previous diagnosis was confirmed, was the name of tuberculosis mentioned for the first time.

When a patient had to leave the factory for sanatorium treatment, the job was kept open for him and he was allowed to return to the factory as soon as his condition was sufficiently improved.

No compensation had ever been asked for tuberculosis by the employees, and none had ever been paid.

Radiographic examination of industrial workers was only justified if the examination was carried out when the worker entered the factory the *first time*, in order to prevent the employment of active tuberculosis cases. This examination should be carried out if possible at a central place where the workers could be sent to, or at the factory itself. Radiographic examination of employees once a year would have very little effect on the spreading of tuberculosis in industry, because newly employed workers suffering from active tuberculosis were likely to infect during work time those who had been tested and found without any lung trouble.

Dr. W. Allen Daley said that he thought the London County Council was the first local authority to use one of the new sets for mass radiography. The capital cost was just under £2,000. The L.C.C. had also hoped to obtain a van and generator, which would have cost another £2,000, but they were not yet available. An important point on capital expenditure was the need for providing movable dressing cubicles which could be taken from place to place.

The cost of maintenance was between £2,000 and £2,500 a year for staff and £1,800 a year for general maintenance, of which films cost £580 and laundry £245.

The set was first used to examine the staff and patients of two large mental hospitals, and as a result a few minor technical defects in the apparatus were discovered and rectified. At one of the mental hospitals it was found in 6·8% of the male and 5·1% of the female patients that large films were needed, and in approximately half of them active, or probably active, tuberculosis was diagnosed. In the other mental hospital in 3·7% of the male and 1·2% of the female patients there were unsuspected pulmonary lesions which required further investigation.

Since October 4, 1943, the set had been used for the general civilian community. Priority was given to scholars of secondary and technical schools and to Civil Defence workers (because they mostly sleep in dormitories). Employees of industrial firms were also invited. In the latter the response varied from 12% to 92% of the staff. In 0·74%

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*January* 28, 1944]

DISCUSSION: ASPECTS OF THE WORK OF THE ALMONER IN A NATIONAL HEALTH SERVICE

Miss D. Manchée (St. Mary's Hospital): There has developed in the mind of the public and in some medical circles also, an erroneous and unfortunate conception of the almoner as someone who has "something to do with the money". This has undoubtedly arisen, not only from the title "almoner" but as a result of her dealing with the assessment and collection of patients' payments.

Briefly, the almoner's training demands a University course in Social Science, followed by fifteen months practical study in family case-work agencies and hospitals, under qualified workers. This provides theoretical knowledge regarding the social sciences and social implications of disease, together with practical experience in home-visiting, interviewing and the keeping of records. The standard of training is maintained by the Institute of Hospital Almoners and their Certificate of "Associate" granted only to those attaining that standard.

Her functions consist of the application of the principles of case-work to the hospital patient, which may be defined as the art of helping people to achieve the fullest possible measure of health and independence. This entails the discovery of the patient's social background; co-operation with the medical staff to enable the patient to carry out the recommended treatment: following-up to re-establish him in normal life, obviating so far as possible a further breakdown; and extensive after-care for the acutely and chronically ill.

More general duties include the supply of appliances, arrangement and supervision of convalescence and home-visiting. To share in the formation of hospital policy, in so far as it affects the patient, is also her responsibility, and acting as a link between the hospital and the various agencies, both statutory and voluntary, which exist for his welfare. This entails attendance at Committees and group discussions while knowledge of the social background and keeping of records are frequently used as aids to medical research.

It will be clear that if this work is to be well done, it requires specialized knowledge. Unfortunately many authorities still concentrate on the raising of money and appoint an almoner with this specific purpose in view. Advertisements still appear in the press, offering vacancies for those "holding the Certificate of the Institute or a University degree or with experience in social work" and even the Ministry of Health in Circular 2232 of December 1940 urged hospitals to appoint "a qualified almoner or some reliable person who has had experience of almoner's work"!

Still unrecognized is the amount of damage which can be done in the patient's home or life, through ignorance or misguided zeal on the part of the hospital almoner.

The almoner service commenced in a voluntary hospital in 1895 and it is natural that, for some years, the voluntary hospital alone experimented with this innovation. The need for the service in the municipal hospitals, however, became apparent after 1929 when the Public Health Authorities took over the old Poor Law Infirmaries: to-day of some 516 almoners in hospital, 315 are employed by voluntary and 185 in municipal hospitals.

In addition to work in the hospitals, almoners are now employed in tuberculosis dispensaries and venereal disease clinics, in maternity and child welfare centres, while some, having taken the mental health course, are working in mental hospitals and child guidance clinics.

Some confusion seems to have arisen lately as to the difference in function between the health visitor and the almoner.

The health visitor's training is that of a nurse, her outlook that of public health. The fundamentals of the almoner's training is the practical application of the social sciences, and her outlook, the social welfare of the individual in relation to his family

Illustrating the opportunities available to social medicine by a mass fluorographic service in a special section of the civilian community in whom the incidence of tuberculosis was likely to be high, Dr. Ellman gave records of a contact service of 2,681 presumably healthy subjects in 9·6% of whom pulmonary tuberculosis was discovered, 6·75% of which were proved to be active lesions. In this same service 0·64% were found to have cardiac lesions, of whom 5 cases were rheumatic, 8 hypertensive and 2 specific in origin [2].

Dr. Ellman regarded it as essential that victimization of workers discovered by this method to have lesions should in no circumstances be allowed to occur, if the scheme were to prove a working proposition. On the contrary, a system of adequate financial allowances should be instituted to enable treatment to be carried out successfully, together with a scheme for vocational guidance and rehabilitation. The Ministry must surely understand that the increased number of cases of pulmonary tuberculosis discovered by this means would require a corresponding increase in the facilities for institutional treatment, although of course by no means all cases discovered would require active treatment. Some selected cases might well respond to initial treatment and follow-up at, for example, "preventoria". Close liaison between existing units and social service departments for the care and after-care of patients would be required. He agreed that any scheme for a fluorographic service for the civilian population of the future should be entirely dissociated from existing tuberculosis clinics.

REFERENCES

1 CLARK, K. C., CORDINER, G. R. M., and ELLMAN, PHILIP (1941) *Brit. J. Radiol.*, 14, 54, 186.
2 ELLMAN, PHILIP (1941) *Proc. R. Soc. Med.*, 34, 595.

Dr. Norman P. Henderson drew attention to the position of the factory medical officer in relation to the medical officer in charge of the mass radiographic unit. A complaint had been received that the latter at one factory had erected a barrier of professional secrecy and had refused to convey any information regarding positive or suspect cases to the cases themselves or to the factory medical officer. It was pointed out that the factory medical officer is under the same responsibility as any other doctor regarding professional secrecy, and he or she is only entitled (with the patient's permission) to convey information regarding disease in members of the factory to the managing director, or his nominee, where it is a matter that affects the health of the unit generally, or alternatively, the individual's efficiency.

It seemed rather nonsensical to carry out mass radiography if the factory medical officer to be ignored. As the law at present stood, the patient could not be forced to accept treatment from his private doctor. If such a person was employed handling proprietary foodstuffs, the danger to his fellow-workers and the general consumers must be obvious. His private doctor might decide "to watch" the case and so the position deteriorated further.

Though the mobile unit was now being successfully employed it would still be necessary to employ static units at fixed centres to cover the many millions of the population who were not conveniently centralized in factories. The policy of training medical officers of health to "spot disease" on miniature films like "young boys spot different types of aeroplanes" was to be deprecated and if persisted in, must sooner or later bring discredit to this important field of chest work destined to revolutionize social medicine. The solution would appear to be to organize a series of examining boards on a regional basis to cover Great Britain and on each board, a radiologist and a physician, both experts in the interpretation of miniature and full-size films. Finally, a central consultative board should be established as a last source of appeal for the very difficult cases.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[January 28, 1944]

DISCUSSION: ASPECTS OF THE WORK OF THE ALMONER IN A NATIONAL HEALTH SERVICE

Miss D. Manchée (St. Mary's Hospital): There has developed in the mind of the public and in some medical circles also, an erroneous and unfortunate conception of the almoner as someone who has "something to do with the money". This has undoubtedly arisen, not only from the title "almoner" but as a result of her dealing with the assessment and collection of patients' payments.

Briefly, the almoner's training demands a University course in Social Science, followed by fifteen months practical study in family case-work agencies and hospitals, under qualified workers. This provides theoretical knowledge regarding the social sciences and social implications of disease, together with practical experience in home-visiting, interviewing and the keeping of records. The standard of training is maintained by the Institute of Hospital Almoners and their Certificate of "Associate" granted only to those attaining that standard.

Her functions consist of the application of the principles of case-work to the hospital patient, which may be defined as the art of helping people to achieve the fullest possible measure of health and independence. This entails the discovery of the patient's social background; co-operation with the medical staff to enable the patient to carry out the recommended treatment; following-up to re-establish him in normal life, obviating so far as possible a further breakdown; and extensive after-care for the acutely and chronically ill.

More general duties include the supply of appliances, arrangement and supervision of convalescence and home-visiting. To share in the formation of hospital policy, in so far as it affects the patient, is also her responsibility, and acting as a link between the hospital and the various agencies, both statutory and voluntary, which exist for his welfare. This entails attendance at Committees and group discussions while knowledge of the social background and keeping of records are frequently used as aids to medical research.

It will be clear that if this work is to be well done, it requires specialized knowledge. Unfortunately many authorities still concentrate on the raising of money and appoint an almoner with this specific purpose in view. Advertisements still appear in the press, offering vacancies for those "holding the Certificate of the Institute OR a University degree OR with experience in social work" and even the Ministry of Health in Circular 2232 of December 1940 urged hospitals to appoint "a qualified almoner or some reliable person who has had experience of almoner's work"!

Still unrecognized is the amount of damage which can be done in the patient's home or life, through ignorance or misguided zeal on the part of the hospital almoner.

The almoner service commenced in a voluntary hospital in 1895 and it is natural that, for some years, the voluntary hospital alone experimented with this innovation. The need for the service in the municipal hospitals, however, became apparent after 1929 when the Public Health Authorities took over the old Poor Law Infirmaries; to-day of some 516 almoners in hospital, 315 are employed by voluntary and 185 in municipal hospitals.

In addition to work in the hospitals, almoners are now employed in tuberculosis dispensaries and venereal disease clinics, in maternity and child welfare centres, while some, having taken the mental health course, are working in mental hospitals and child guidance clinics.

Some confusion seems to have arisen lately as to the difference in function between the health visitor and the almoner.

The health visitor's training is that of a nurse, her outlook that of *public health* The fundamentals of the almoner's training is the practical application of the social sciences, and her outlook, the social welfare of the individual in relation to his family

and environment. It would be a sad loss to both, and calamitous to the patient, if through lack of understanding, the authorities were to breed any form of rivalry between these two useful bodies.

Although some almoners believe it to be their duty to assess the patient for payment, on the ground that it is she who knows his situation fully, the other school, to which I belong, believes that this work is outside the scope of an almoner's duties. It tends to increase the patient's reserve concerning his affairs, and most important, allows too little time for the detailed study of individual environment.

At St. Mary's for example, assessment and collection of patients' payments is undertaken by a special Patients' Contributions Office, whose records are available to the almoners, who were relieved many years ago of these duties. This office also deals with claims under the Road Traffic Act, with the various contributory schemes and with the transfer of patients to other hospitals.

Relieved of these duties, which at present constitute the main tasks of some almoners' departments in other hospitals, our time is available for the development of various specialized forms of social work.

The department consists of eight full-time qualified almoners and we endeavour to see all patients in wards and clinics, with a view to ascertaining whether they understand and can carry out treatment or whether help will be necessary; and if so, in what form. In the case of in-patients, the almoners go armed with the knowledge, obtained from the Contributions' Office, of financial circumstances, and of the assessment, which they can, if necessary, get adjusted. Out-patients are asked to state their circumstances with a view to assessing *need*, while care is exercised to avoid the abuse of hospital and medical services by those capable of making their own arrangements.

In addition to the out-patient clinics and wards, almoners work in the venereal disease department, the diabetic, casualty and fracture clinics. All cancer patients are cared for, whether life is of long or short duration, home-visiting and after-care being available for all patients in need. Almoners attend, as representatives of the hospital, on the committees of the local case-work agency, Invalid Children's Aid Association and Tuberculosis Care Committee.

Contact is maintained with almoners at the Base Hospitals to ensure continuity of social and medical care and the service is extended to include necessitous air-raid casualties. In addition visitors are welcomed; this year's students have included parties from the Royal Institute of Public Health and Hygiene, the women of the Free French Forces and groups from various social bodies.

Of recent development is the teaching of social medicine to medical students and nurses. Experiments are being conducted in many hospitals in talks by the almoner, in practical demonstrations and in participation in the ward round for the contribution by the almoner of the patient's social background.

These are some of the ways in which the almoner can take part in a National Medical Service, and since in some quarters the need of her help has been for some time apparent in private practice, the health centre, comprising a group of such doctors, would make an excellent pivot. In outlying country districts she could well act as a liaison officer, her services being available for more than one health centre and to the general practitioners of the surrounding district.

The appointment of an almoner to the staff of the Ministry of Health would go far in developing the service on a co-ordinated plan throughout the country.

Mr. E. Ridley (Director of Public Assistance, Middlesex County Council): Since 1930, when the public assistance hospitals and institutions were transferred to County and County Borough Councils, a number of such authorities have engaged hospital almoners. Public Assistance Authorities are obliged by law to recover from the patient and any liable relatives contributions towards the cost of the patient's treatment in hospital according to their financial ability. A similar duty rests upon the Public Health Authorities for treatment in public health hospitals. This duty has naturally influenced the work of the almoners engaged in these hospitals. Almost invariably they have to undertake the work of obtaining from patients particulars as to their financial circumstances and the names and addresses of liable relatives. Usually this information is transmitted to another official who completes the inquiries and fixes the amount of the contribution.

At some hospitals admissions are arranged through the almoner's department but this is not a general practice. There is one type of patient for whom the almoner is unquestionably the best means of admission, i.e. expectant mothers. In Middlesex, those who require hospital treatment either on medical grounds, or because they are too poor to bear the expense of a confinement at home, or because their home conditions are unsuited for a confinement, are given priority. The almoner inquires into their cir-

cumstances under these several heads, and arranges for their admission. In public assistance hospitals the almoner co-operates with the voluntary agencies in dealing with the unmarried mother. She not only arranges admissions but gives the mother every help in her difficulties of affiliation, adoption, or finding a fostermother for the baby, or the supply of baby clothes. She also helps the mother in her return to independence.

It is generally the practice in Poor Law and Municipal Hospitals where out-patient departments have been established for the almoner to carry out the administrative work, and in most cases also to obtain contributions from out-patients. They also put the patients in touch with outside organizations.

Almoners have been found very useful in obtaining for the medical staff information respecting the home environment of persons where such knowledge is of value for treatment. They also assist patients in dealing with their sickness benefits, pension forms, or Hospital Savings Association vouchers.

The requirements of Poor Law and Municipal Hospitals regarding the recovery of the cost of maintenance from patients and relatives throw upon the almoner a good deal of work connected with financial inquiries. It is a pity that this is so, as it detracts from the almoner's value in the more important functions of restoring the health of the patient and of the patient's subsequent reinstatement as a healthy member of the community. However, it is very difficult to find anyone more suited than the almoner to approach the patient in the first instance regarding repayments.

If, as Sir William Beveridge envisages, there will be no charge for treatment and merely a token charge for maintenance, for which he suggested a sum of say 10s. per week, then the functions of the almoner in regard to financial inquiries and the like should disappear. But the welfare work carried out by almoners to-day will still be needed under the new service.

The work of rehabilitation, as well as the kindred subject of occupational therapy, are likely to affect the almoner very considerably, at any rate in the early stages, though these therapies may become so important in the future as ultimately to require their own special organization.

Dr. J. A. Charles (Medical Officer of Health, Newcastle-upon-Tyne, C.B.): To follow the development of the science of social administration in this country from its beginnings is to realize the gentle inevitability of English forms and institutions.

As throughout our history the occasion has rarely failed to produce the man, so in the story of our sociological progress the movement has generally evolved its desired instrument, the suitable tool, the appropriate agent or officer.

From that strange mixture of savage oppression, practical philanthropy, and experimental economics which marked the successive stages of the Elizabethan Poor Law, came the overseers or collectors, who with their virtual descendants, the relieving officers, may possibly be acclaimed as the first lay English social workers. Ruskin and the humanitarian housing projects of the mid-Victorian period produced Miss Octavia Hill and in her train the enlightened and competent group of housing managers.

For ten years Sir Charles Lock foresaw the need for the services of a charitable assessor in hospital—"a person well instructed in all forms of relief other than medical." In 1895 came the first hospital almoner. From that moment we can date the combination of organized medical and social service in the hospital, and its subsequent expansion and extension are the phenomena of normal growth. Two years earlier, in 1893, the Lancashire town of St. Helens appointed a female sanitary inspector. Other local authorities followed, until by 1905, 45 towns were employing a female staff of this kind. Their duties included the examination of the working conditions of women and children in industry, the follow-up of cases of infectious disease, the inspection of slum houses, the supervision of midwives and the visiting of newly-born infants and their mothers.

At first these inspectors were often not nurses, but gradually as their work became more and more concerned with women and children, it was recognized that a nursing training, with or without the sanitary inspector's certificate of the Royal Sanitary Institute, was the essential qualification. In certain towns the credit for introducing this new form of social worker must be given to forward-looking but ambiguously named bodies—the Ladies' Health Societies.

Very soon the title of the female sanitary inspector was changed to health visitor, and their first homely kitchen meetings were the forerunners of the maternity and child welfare clinics of to-day.

It would have been too much to expect that these several categories of social workers should refrain from seeking to perpetuate themselves by formulating specialized courses

of training for those anxious to be admitted to the mysteries. They forgot in doing so the advice of Samuel Butler that the specialist must always be a bit of a general practitioner, and that the general practitioner should aim at a modicum of specialization. This criticism applies equally to the almoners and health visitors (or rather to those responsible for their training).

Against a university background the almoner-to-be (who has been carefully selected by a board quick to detect actual or potential deficiencies in the candidate) acquires a knowledge of social history and policy, social psychology and its application, public administration and cognate subjects. Later she welds academic theory to practice in her training in family case work under the tutelage of the Charity Organisation Society or other similar family case-work body, and completes her apprenticeship in the almoner's department of a hospital or hospitals. At the end of a minimum period of three years, she stands out as an individual educated in the principles of social administration, and possessed of the rudiments of a technique which experience and practice will bring to perfection. She has had the advantage of an education, purposefully directed to one end from its commencement.

So equipped, she embarks upon her calling and, in many instances, discovers that her employers have an incomplete, if not a misdirected, idea as to her function. Despite their protests there are still too many almoners tied to the financial wheels of a hospital, rather than yoked to its purpose of medical and social service.

In order that she shall be of the greatest possible assistance to the patient, the almoner must be aware of his economic position. That information once obtained cannot unfortunately be considered by the almoner *in vacuo*. She must also concern herself with the financial nexus which links her employer, the hospital, to her client, the patient. There are many sources of physical, mental and social disease—the problems and incompatibilities of family life, the maladjustment of the worker to his employment, the ill-considered consumption of time and money in the pursuit of happiness—which require investigation. And in the unravelling of these problems the almoner could do much.

The health visitor has an entirely different vocational genealogy. She has followed the arduous uphill path which leads from novitiate to fully-trained membership of the nursing profession. Along that road she has met human beings in the extremities of bodily and spiritual need; she has learned to minister to them. Thereafter for a short period she acquires some knowledge of midwifery, and in so doing makes contact with the day-by-day life of homes and families other than her own. Finally she elects to commence the concentrated and conglomerate six months' course for the health visitor's certificate of the Royal Sanitary Institute or other recognized body. During this period, apart from gaining practical experience in the basic duties of the health visitor—domiciliary visiting and attendance upon pre-natal and child welfare clinics—she receives instruction extending over some 160 to 180 hours in a series of subjects. This includes *inter alia* physiology, food and nutrition, elementary economics, vital statistics, pædiatrics, tuberculosis, thrift needlework and the general principles of sanitary law and administration. With this armamentarium to draw upon it is not surprising that the certificated health visitor has been invited to undertake dietary surveys, write housing reports, act as a mass observations visitor, and report upon mental defectives—all of which tasks she has accomplished with competence and distinction. Educated as a nurse, and provided with the technique of that calling, she becomes also the repository of a heterogenous collection of pieces of information. Her vocational training fits her to deal supremely well with the medical aspect of a number of human problems; her ancillary instruction, for all its catholicity, does not necessarily enable her to diagnose the social factors which may be involved, or to assess their significance. I have made a point of this antithesis—the almoner on the one hand, the health visitor on the other, in order to underline their respective strengths and weaknesses, capacities and competence.

I now turn to the field of medico-social work which lies outside the hospital, but within the sphere of the local authorities.

In a normal year in the City of Newcastle, approximately 13,500 individuals, men, women and children, are admitted to the voluntary, municipal and private hospitals out of a population of 300,000. (Patients suffering from tuberculosis, infectious and mental diseases are not included amongst these admissions.) In addition, some 16,000 new out-patients, all Newcastle inhabitants, attend the various out-patient departments of these hospitals. There is thus an annual total of 29,500 potential clients for the services of the six hospital almoners working in the city hospitals.

If we consider the activities of the local authority, as exemplified in its ante-natal, infant and toddler clinics, in the tuberculosis dispensary, in the out-patient clinics for psycho-neurosis, and in the venereal disease department (all other personal health undertakings

of the municipality being excluded) we find that on an average some 11,000 individuals present themselves as new cases.

Until five years ago there was no provision for any investigation of the social background of these patients, except for such as could be carried out by the health visitors, or in the case of tuberculosis, by the Voluntary Tuberculosis Care Council. The facilities for investigation were slender, and the good-willed attempts to solve the medico-social problems which came to light were often ineffectual.

I think one can say that the health visitors recognized that however helpful and purposeful their advice might be to the expectant or nursing mother, or to the patient returning from a sanatorium to poor home conditions, it was inadequate in many cases because they personally were unable to elucidate precisely the familial, industrial or economic factors involved, and, *a fortiori*, to prescribe the appropriate social therapeusis.

My submission is that in the ordinary routine work of the official personal health services there is an abundance of human material for medico-social treatment. Very often the immediate need which sends the individual to the child welfare centre, the tuberculosis dispensary, or the venereal diseases clinic is only partially relieved by the therapeutic methods adopted in those departments, and wholly successful treatment is only possible when the underlying ætiological factors, be they economic, familial, industrial or psychological, have been discovered. It is at this point that the medical practitioner, the health visitor, the tuberculosis nurse join hands with the almoner, and in some cases with the psychiatric social worker. For the former group it is not a confession of failure, but a recognition of the existence of another technique, and the acceptance of the thesis that the treatment and education of the patient and his family require the co-operation of medical, ancillary and social workers. For the almoner it is an opportunity to move beyond the hospital and to see, through personal domiciliary visitation, the actual operation of some of the contributory causes of disease.

There remains the province of the family doctor. Hitherto this field has only rarely been open to the almoner. It is obvious, however, that there are many ways in which she can co-operate with the practitioner in ensuring the fulfilment of his recommendations not only as regards medical treatment, but in providing assistance of various kinds and in improving the social and economic background. The average general practitioner has to rely on the agent of Friendly Societies, the local Council of Social Service (if he is aware of its existence), the parish priest, or his own mother-wit to provide different forms of social service. It is my opinion that in every large area the general practitioner should be able to refer patients requiring social investigation and treatment to an almoner, just as easily and as confidently as does his colleague on the staff of a hospital.

We have then a large mass of medico-social problems lying ready for solution in every community. It will be necessary for the complete efficiency of the National Health Service that they should be adequately handled, and in my opinion the proper person to attempt the task is the almoner. Obviously she will not work alone, but as a member of a team which will include the hospital or doctor, medical staff of the several health services, the health visitor, the psychiatric social worker, the district nurse, and the school teacher.

I would tentatively suggest that the extra-hospital establishment should number approximately two-thirds of the hospital establishment. In other words, if nine almoners are requisite for the hospital needs of a town of 300,000 persons (and I myself believe that this is near the mark) then an additional six can be employed outside the hospital in relation to the maternity and child welfare service, the tuberculosis dispensaries, the venereal disease clinic, the orthopædic clinic, the school services and the work of the general practitioner whether based on health centres or otherwise. I have excluded the psychiatric social worker and her sphere from this computation.

As to the work of the individual almoners, I would suggest that this should be specialized within limits. Certain almoners should concentrate on the problems of the tuberculosis dispensary, for example, but there should be annual interchange of work within the health service, and almoners should also move from the hospital into the extra-hospital field and vice versa.

The health service almoner should be mobile, undertaking domiciliary visits whenever necessary. In her relations with the medical practitioner she should act as if she were a consultant called in to advise and offer guidance on some aspects of the case—the social or familial or industrial or economic aspects.

For the proper conduct of her work it is essential that the almoner should be provided with the elementary conveniences—office accommodation and clerical assistance.

Finally, whatever the form and scope of the Almoner Services, they must be dovetailed into the organization of the National Health Service as a whole.

In my earlier remarks I sought to convey the impression that by reason of their different equipment it would be unwise and wasteful for the almoner to attempt to replace the health visitor, or for the latter to assume the functions of the almoner. Their respective tasks and responsibilities are complementary, and personally I find that this arrangement works well; each realizes the limitations of her office and is aware of the greater benefit to the patient that is achieved by co-operation. Whether this division of one large medico-social field should continue is another matter.

Competent observers have suggested that the American Public Health Nurse, with her slightly less comprehensive nursing training and her broader social education, is an instrument of more general utility than either the almoner or the health visitor. I will only say that even if it be shown that some new species of ancillary officer must ultimately be evolved, no harm can be done and much good will accrue if, at an early date, the training of the health visitor is stripped of its non-essentials and the new curriculum is reorientated so as to catch the light from both the medical and sociological quarters of the heavens.

For all our social workers there can be no better rule of life than that of John Wycliffe—keeping the hests of God, doing the works of Mercy, ruling well their five wits and doing reason and equity and good conscience to all men.

Miss M. J. Roxburgh (Institute of Hospital Almoners) hoped that steps would be taken to guard against the home being invaded by too many visitors.

Dr. C. Fraser Brockington (Medical Officer of Health, Warwickshire) thought that the problem of the almoner's functions in a National Health Service so far as it related to extra-hospital work required very careful consideration in view of the existing Health Visitor Service. He considered that there was no doubt that the health visitor was a social worker in that she "had personal contact with individuals and families in the community in need of guidance and help" and in fact the more she fulfilled the function of social worker the better health visitor she would be. That she was an ideal social worker was not contended and with our growing appreciation of the value of attention to the personal problems of individuals and families it was evident that an effort would have to be made to extend her capabilities in this direction. Before introducing a new type of social worker into "the field" it was as well to bear in mind how many different varieties might now visit persons in their homes. There did not seem to be any need to limit the number of social workers providing each had an individual and distinct function with a minimum of overlapping, but it was important to avoid two types of person with different forms of training undertaking substantially the same work. A further point to be borne in mind was that certain classes of social work require the basic training of a nurse, those in which the principles of preventive medicine, e.g. epidemiology and child care, are involved, as in the tracing of venereal disease contacts and defaulters or in schemes for the care of illegitimate children; there could be no doubt that in such specialized forms of social work the almoner would be at a disadvantage. It might be found desirable to combine and modify the training of the health visitor and almoner to produce one person of the type of the public health nurse known in the States. On the whole, however, the best line of approach would probably be to make use of both: the health visitor should be more of a social worker and her training improved to meet this: almoners should be appointed to public health departments to undertake more investigations of certain types of case referred from health visitors or other social workers.

Miss Manchée, in reply, thought that, in spite of the misconceptions to which the term "almoner" gave rise, there was little to be gained by changing it at present.

Section of Orthopædics

President—S. ALAN S. MALKIN, F.R.C.S.Ed.

[*November 2, 1943*]

The Contribution of Orthopædic Surgery to Hospital Development

PRESIDENT'S ADDRESS

By S. ALAN S. MALKIN, F.R.C.S.Ed.

LIKE many others qualified in the last war I joined the R.A.M.C. and spent the first years of my professional life in the Army. As a regimental medical officer I saw the method whereby a man who became sick or wounded, wherever this sickness or wound might have occurred, was sent through the appropriate channels to the place where he would receive the proper treatment. I saw that there was, in fact, an organized system for dealing with every case according to its needs.

At the conclusion of the war I became keenly interested in orthopædic surgery, and it was because the national plan of the late Sir Robert Jones and G. R. Girdlestone (*Brit. med. J.*, 1919 (ii), 457) showed a need and gave an organized method that it made a great appeal to me. More than that: it seemed to me that it could be used—in addition to providing treatment for crippled children—as a small scale experiment in hospital organization. It could, in fact, be regarded as a long-term tactical exercise carried out in real life with its special and its general ideas—the special to provide orthopædic treatment, the general to make a contribution to hospital development. If only the special objective were reached, the effort would have been worth while.

The scheme in brief was this: The division of England and Wales into a number of districts; the establishment in each district of an open-air, country orthopædic hospital and a system of scattered out-patient clinics; the organization of efficient treatment and a general co-ordination by a committee working under the Ministry of Health.

In 1923 the Nottingham Cripples' Guild appointed me orthopædic surgeon to develop a scheme on the lines of Sir Robert Jones' national plan. At that time, the Guild had a very small clinic, consisting of one room for treatment by physiotherapy and some offices. Superficially, the outlook was certainly not very bright, but the President of the Guild was the Duchess of Portland, who was most enthusiastic and ready to do anything to help, there was a Committee which had a real desire to do something for cripples, and one member, a lawyer, the late J. W. Briggs, who had had considerable experience in both legal and charitable work and who was heart and soul in the project. It was an encouragement to remember that to such a combination as this, representing nearly all sections and strata of society and imbued with a common desire to help their fellow men, most of the social enterprises in England owe their origin.

There were, on the books of the Cripples' Guild, a number of cripples and amongst them were found some who, it was thought, could be benefited by orthopædic treatment. Amongst the cases labelled physically defective on the books of the City School Medical Inspection Committee were found a large number requiring treatment.

For out-patient treatment I had the help of a masseuse and a nurse trained in orthopædic nursing, and Naughton Dunn allowed me to have, as a temporary measure, eight beds, ultimately increased to forty, at St. Gerrards Hospital, Coleshill, about fifty miles

from Nottingham, which were all paid for by the Nottingham authorities, public or private. I visited the hospital once a week to operate and make ward rounds.

In 1926 a new clinic was built in Nottingham with funds raised by a public appeal. It contained offices, plaster rooms, physiotherapy department and accommodation for a workshop.

Ultimately six voluntary clinics were established. Each had its own voluntary committee and was responsible for providing the maintenance, either by direct arrangement with the public authorities or by raising the funds in some other way, of each patient in its own area requiring orthopædic hospital treatment. Each was permanent and was open at least three times a week for treatment. I visited each clinic in the small districts once a month, and in the two larger areas twice a week. In the area covered by each clinic a follow-up system was organized.

An essential part of the scheme, however, was the provision of an orthopædic hospital to serve the needs of the region. For this again a public appeal was made and as a result the Harlow Wood Orthopædic Hospital was built. In 1929 it was opened to serve primarily Nottinghamshire, the north of Leicestershire and parts of Lincolnshire. It was gradually enlarged from 80 beds to 155 beds, which included a small block for private patients.

In the plan, three points are of special interest. The first is the arrangement of the wards in relation to one another and to the administration block. The wards are in echelon and at an angle to the administration block. By this means each has a southerly aspect but the frontage is reduced and the plan made more compact. The second is the arrangement of the children's ward, which can be divided into four independent units and has isolation rooms at each end. The third is the inter-relationship of the plaster room, theatre and X-ray departments.

When the war came, the Ministry of Health, by agreement with the Committee of the hospital, acquired for its wards and ancillary buildings on the hospital's grounds sites, with the right of access, on a twenty years' lease at a peppercorn rent. On these sites the E.M.S. buildings were erected. With these additions the hospital is able to accommodate 355 patients. It also controls an annexe of fifty beds, which is used as a rehabilitation centre, and has linked with it two British Red Cross Society auxiliary hospitals. This provides another 120 beds, making a potential total of 525, and it is likely that by the use of a further annexe the number may be increased to about 600.

There are some points about the hospital and its organization which should be mentioned:

Control.—The hospital is a company, registered under the Companies Acts, limited by guarantee and not having a share capital. This means that the control of the hospital is vested in the Executive Committee and no trustees are needed. The objects of the Company are clearly set out in the memorandum of association and include treatment, education and training.

Finance.—Apart from the cost of the E.M.S. buildings, all the capital required by the hospital has been raised by voluntary means. It has, however, looked to the Clinic Committees to provide the cost of maintenance of all patients from their own areas. From areas in which clinics do not exist maintenance has been paid either by public authorities or by other interested bodies or by contributory schemes. There are serious gaps in this system which would be closed by the adoption of a national and comprehensive contributory scheme.

It will be seen that the hospital has raised funds for capital expenditure but not for maintenance—which it has received on the basis of payment for work done and not as subsidies.

Co-operation with Government departments and local authorities.—The hospital is recognized by the State and the Staff has to be approved. As a hospital school it works in co-operation with the Board of Education. The local authorities have the right to visit the patients for whom they are financially responsible and to obtain reports on their progress. Representatives of the Ministry of Labour visit the hospital to interview patients who may require training.

The Government has no control over the work or the policy of the hospital, which is autonomous. It is not subsidized by the State but is paid only for services rendered. The question of State control, therefore, does not arise.

Staff.—This consists of a full list of consultants, all of whom are available as and when required and are paid for each visit, and a central Staff of orthopædic surgeons paid on a part-time basis.

The latter are responsible for the work of the hospital and the clinics within easy access. There is also an associate orthopædic surgeon whose main work is in two populous outlying towns in the region and the areas surrounding them. He treats his acute and short-stay cases locally, but sends his long-stay cases or those requiring special rehabili-

tation to Harlow Wood, which he normally visits himself once a week. In the meantime, these cases are supervised by the central Staff.

Under the E.M.S. scheme the hospital is visited regularly by a consulting plastic and a consulting neuro-surgeon.

It can readily be realized that the essential for success in this is team work.

Almoner.—The almoning work is divided into two sections—one section mainly in the hospital and the other in the region.

In the hospital the almoner's duty is to help the patients with advice in domestic or other difficulties that may arise. She forms a link with the Ministry of Labour for any who are likely to require training. She is mainly concerned not with collecting money from patients but with assisting them.

In the region the almoner's duty is to assist in the development of an organization in parts which have not so far been successfully covered, to create interest in the work, and to act as a co-ordinating factor. So important is this considered to be that the Nuffield Trustees recently appointed an almoner for this special purpose. Her work has been suspended on account of the war.

Rehabilitation.—A complete scheme for what is now known as hospital rehabilitation has been developed. It covers not only the rehabilitation annexe but also the associated B.R.C.S. auxiliary hospitals, which have an important part to play in the organization. They are used for specially selected cases—each has a physical training instructor and is visited regularly by a member of the Staff of the hospital. Nearly all Service patients who are expected to be fit for full duty go finally to the rehabilitation annexe which is really a hardening centre.

Vocational training.—Vocational training has not kept pace with the other work of the hospital, but recently land has been purchased on which to build a vocational training centre. It is hoped that this will be commenced shortly and will provide for patients who are unfit to return to their pre-accident work or for others requiring training to enable them to be self-supporting.

This scheme which I have detailed shows how hospitals controlled by voluntary committees can preserve their autonomy and yet co-operate fully with the State, and how voluntary regional hospitals can work with many different local authorities and make their services available throughout the whole region. It also shows how the staff of hospitals in outlying districts can be associated and linked up with the central hospital. Segregation and team-work, which are an integral part of the scheme, make possible still further advances. But this is on one condition only—that we are determined to bring more of the scientific spirit into our work, and to prove by scientific methods all that can be so proved. There is one difficulty which is almost constitutional, and it is this: most of us, if we coldly and clearly look into our minds, have to agree that, in the main, we regard our work not as a branch of science but as what has been called a practical art.

The late Wilfred Trotter, in an essay on "Observation and Experiment and their Use in the Medical Sciences" ends thus: "To the experimenter immersed in his research, and to the clinician struggling with the load of experience and the needs of his patients, it may seem unpractical to concern ourselves with the theory of medical knowledge. On the other hand, it is, perhaps, the lack of rational doctrine and a general interest in the problems of method that has made medicine the scene of so much disunited and contradictory effort and has helped to put it down from its historical position as the mother and nurse of science." This is, indeed, profoundly true and a source of weakness. From the scientific outlook and the interest in method follows the desire for research, for which the regional hospital, with its segregation of cases and a staff not too occupied with routine work, is eminently suited. How such work can be done is shown by the Peripheral Nerve Unit of the Wingfield Morris Orthopædic Hospital.

We all know that the easy days of isolation, whether of nations or of individuals, are gone. If we, as the representatives of our country in our own sphere of work are to pull our weight in the world, we know that we can no longer depend merely on natural ability but must look much more than before to co-ordinated, organized and united effort with a sense of purpose.

This, then, is my conclusion: the plan advocated by Sir Robert Jones nearly a quarter of a century ago has pointed the way to a method of co-operation with the State, to a method of providing specialist services throughout the country, and to one road by which we can make advances in the science and art of medicine. We can, therefore, claim that orthopædic surgery has made a real contribution to hospital development.

The President showed the following lantern slides:

(1) Map of England and Wales, 1924, showing that only three orthopædic schemes were then in existence.

(2) Photograph of Out-patient Clinic in Nottingham.

(3, 4, 5, 6, 7 and 8) Views of the site and wards of the Harlow Wood Orthopædic Hospital.

(9 and 10) Plans of ward blocks.

(11) Plan of administrative block, showing inter-relationship of plaster room, theatre and X-ray department.

(12, 13, 14, 15) Occupational therapy during the first World War.

(16) Use of a loom for exercising the shoulder.

(17, 18, 19) Earliest Rehabilitation Centres : Site of the Asklepieion on the Island of Cos. The Hieron at Epidaurus (near Athens). Plan of the Hieron at Epidaurus, showing baths, gymnasium, stadium, library and hostel.

(20) Map of England and Wales showing the orthopædic centres in 1936.

Orthopædic Surgery and the Future [*Abridged*]

By HARRY PLATT, M.D., M.S., F.R.C.S.

IT is clear that some of the greatest achievements in *preventive medicine* will be the by-products of *social* measures. If to this be added the large scale reduction in the incidence of controllable disease the field of *curative medicine* is certain to undergo contraction. This change will take a generation or more to come about. But now is the time to begin to foster that change in outlook which the doctor of the near future must acquire—i.e. the biological and sociological approach to the problems of health and disease.

The *general practitioner*, as I see him, will have the primary care of the family unit in health and in disease. His main pre-occupation will be the study of the phenomena of the early deviations from the normal rhythm of mental and physical health at all age-periods. He will treat disease in its earlier and reversible stage. He will I believe work more with his brain, for much of the craft procedures in medicine can and should be carried out by medical auxiliaries acting under his direction. General practice will thus become an important specialism—perhaps the most important of all. In the field of *specialist practice* based on a co-ordinated hospital system, with the aid of biophysics and biochemistry, the physician should regain much of his old predominance over the surgeon. But we may be assured that advances in surgical technique yet to come, combined with still more effective measures to "make the patient safe for surgery", will enable the surgeon of the future to invade almost any region of the body with increasing impunity. There is, however, one proviso—that it be necessary for him to do so for the mitigation or cure of a particular disease. What must surely happen is that the newer medicine will supplant the relatively crude surgical procedures used to-day in the treatment of many disorders of the viscera and ductless glands. The future looks rather grim for the abdominal surgeon! But this change in the balance of power will have an equally great repercussion on the repertoire of surgical feats of the orthopædic surgeon. The conservative surgery of accidents and of congenital deformities will no doubt long endure. The surgeon of the future, if he is not to become a mere craftsman in an ever-diminishing sphere, must not only be grounded in the basic sciences and in medical science, but must keep abreast of expanding knowledge in these disciplines. His approach also, to the problems of disease, must be that of the physician-biologist.

Of the more immediate issues which concern the future of orthopædics, there are three problems on which I might offer comment: (1) The scope of orthopædic practice in the near future; (2) the place of the orthopædic surgeon and of orthopædics in the teaching of undergraduates; (3) the training of the orthopædic surgeon.

Future scope of orthopædics.—Will the sphere of action of the orthopædic surgeon remain relatively stabilized for some time to come? That definition of our specialism which we inherited from our great master Robert Jones is conceived in terms of therapeutics: "The treatment by manipulation, operation, re-education, and rehabilitation, of the injuries and diseases of the locomotor system."

To complete the description of our rôle, it must be added that in the exercise of our diagnostic functions we are called upon to act both as a court of first instance and as a court of appeal.

The evolution of specialism in all fields of human knowledge has consisted in the abstraction of parts from the greater whole. Thus, from general surgery (in its nineteenth century connotation as the whole of surgery), orthopædics, urology, thoracic surgery, neurosurgery, and plastic surgery, have each in turn been abstracted. Of these special fields orthopædics is by far the largest abstraction and in scope and importance is analogous to neurology as the largest abstraction from general medicine. Now the natural

trend is for the process of abstraction to continue. Thus in orthopædics at the present time we can detect the tendency to isolate the treatment of injuries of the locomotor system—(the surgery of accidents) as a future "sub-specialty" for a limited group of orthopædic surgeons. This trend, arising within our own ranks and under our own guidance, has received powerful reinforcement from the outside, consequent on the enhanced importance of industrial medicine. We may also contemplate a potential modification in our sphere of activity resulting from the organization of *arthritis centres* in a national scheme for the study and treatment of the chronic rheumatic disorders.

These two examples suggest that whilst the field of practice of any individual orthopædic surgeon may tend to contract rather than expand, the collective responsibility of "orthopædic surgeons" may come to dominate an even wider field than to-day. We have to remember that whereas orthopædics is in one sense an established field of specialist practice, the principles of orthopædics are a concept which should pervade the whole fabric of medicine and surgery. Such general principles as the application of rest and fixation in the promotion of the repair of injured tissues, in the control of infection, and in the prevention of deformity and contracture; the use of purposive movements in the restoration of function are common property. I would suggest, therefore, that the changes which I have touched upon do not point to a disintegration of our special province, but rather to a wider diffusion of our influence and teaching in Medicine as a whole.

Orthopædics in undergraduate teaching.—The aim of all undergraduate teaching is to turn out a doctor who after a further period of postgraduate training is fit to enter general practice. But in the wards of the medical side of the teaching hospitals, the student is still confronted with the late results of disease, with large numbers of clinical rarities, and with syndromes labelled as specific entities. On the surgical side, the atmosphere tends to be dominated by the dramatic circumstances attending feats of major surgery. The whole setting is designed—unconsciously no doubt—for the training of the specialist. The basic themes of the content of the clinical education and training of the undergraduate as I see them are as follows: (1) The *meaning* of symptoms and signs in the context of discovered physiology and anatomy; (2) the natural history of disease—not of specific diseases. In Henry Cohen's words—"There are no diseases, there is only disease"; (3) the response of the patient to the special influence of his heredity and environment. It should be repeatedly impressed upon the student that the clinical picture observed in the casualty department, out-patient clinics, and in the wards, is an episode. With this approach, the picture of established and relatively incurable disease, which must for a long time form so much of the clinical material of the teaching hospitals, can be presented to the student in true perspective. All teachers will thus in their respective spheres teach social medicine.

Now if this concept of the aim and content of clinical teaching be accepted, it is obvious that the orthopædic surgeon who deals with perhaps the widest single field in medicine—the disorders of the locomotor system—has just as much to offer to the student as any other clinician whether bearing the title general or special. I would therefore maintain that the orthopædic surgeon must take a large share in undergraduate clinical teaching throughout the three clinical years. He will not teach as a specialist, or attempt to teach something regarded as a specialism in the narrow sense of the term. He will certainly not teach orthopædic *surgery* to undergraduates, but he will teach *orthopædics*, first as a notion in clinical medicine, and second in its special application to the wide field of disorders of movement and locomotion, with all its biological and sociological background. The same status and responsibility in undergraduate education must clearly be accorded to all heads of the larger clinical departments. But it may be asked—who will teach general medicine and general surgery? or, who will teach general principles? The answer is plain. In the first place there are no men to-day—under the British hospital system—omniscient and omnipotent, capable of teaching general medicine or general surgery, i.e. the whole of medicine and the whole of surgery. And secondly, all specialist teachers, if fit to be University teachers at all, are in a position to present general principles in the most illuminating fashion. There remains the problem of the co-ordination of the collective effort of a group of "specialist" teachers. The titular head of a university department of medicine or surgery must be primarily a specialist of distinction in one field of clinical action. He must also be a scholar of wide learning and culture. I would here stress my own strong personal conviction that the direction and co-ordination of the larger strategy of undergraduate teaching is not the function of a Clinical Dean.

The training of the orthopædic surgeon.—Both the Association of Surgeons of Great Britain and Ireland and the British Orthopædic Association have submitted progressive views on this question to the Royal Colleges. My own version of the ideal scheme of

post-graduate training may be briefly summarized. The period of training for the would-be surgeon falls naturally into two main stages:

(1) *A preliminary stage*, common to all, immediately following qualification and consisting of a combination of varied clinical training in junior resident posts and higher education in the basic sciences. This stage would cover a period of three years and would culminate in the obtaining of the requisite higher diploma of one of the Royal Colleges.

(2) *A second stage*, the period of true apprenticeship, as a whole-time resident surgical officer, registrar, or chief assistant. For the intending orthopædic surgeon, one year of this period should be spent in a "general surgical" unit, where the experience gained will be mainly in the classical field of visceral surgery, and cancer surgery in general. After that he should spend not less than *three* years as resident surgical officer in a large orthopædic hospital, or as whole-time assistant in the orthopædic department of a large general hospital. In university and teaching hospitals a longer apprenticeship is desirable, so that during this period, the chief assistant can be seconded for travel for six months, or exchanged with his opposite number in a clinic of equal standing at home or abroad.

The future University teacher should receive special training in experimental and clinical research. Only at the end of the full period of training should the young orthopædic surgeon be eligible for registration as a consultant or specialist by a central academic body set up for this purpose.

It is the duty and responsibility of those entrusted with the training of the orthopædic surgeon of the future to ensure that we recruit and educate as high a proportion of scholars and teachers as any other of the major specialisms in medicine and surgery.

Section of Psychiatry

[November 9, 1943]

Neuropsychiatric After-Effects of Cerebrospinal Fever

[Abridged]

By M. NARASIMHA PAI.

DURING the last few years a number of papers have appeared on cerebrospinal fever but comparatively very little has been written on the neuropsychiatric after-effects, sometimes observed in a few patients.

The epidemic of 1940 afforded a suitable opportunity, and it was decided to study a group of patients in order to determine the nature of their disorder, whether their illness differed in any respect from the neurosis commonly seen in war time, and whether there was sufficient data to postulate an infective cause for the origin of their symptoms.

In a survey of neurosis among 8,700 Service patients and 1,635 civilians of both sexes referred to a neurosis centre for neuropsychiatric investigation and treatment, there were 54 patients who gave a history of cerebrospinal fever. Of these 20 had their illness in childhood. Two, who had their illness in 1938, will be considered separately. The remaining 32 patients had all been examined and recommended for admission by psychiatrists.

The average age of the 32 patients was 24, ranging from 18 to 31. The history, as obtained from various sources, was in 13 cases of a mild attack not causing any greater disturbance than headache, malaise, slight fever and neck rigidity. In 19 the illness had been severe and 12 of these had disturbances of consciousness, mainly delirium. No history of delirium was obtained in 7 of the severe cases, 1 had his illness in 1939, 17 had it in 1940, 11 had it in 1941 and 3 within the last two years.

On admission the Wassermann reaction, the E.S.R. and the Group intelligence tests were done as a routine. In addition 5 patients had psychological tests for intellectual deterioration and 6 had their E.E.G. done. Rorschach tests were given to 2 patients.

Ætiological factors.—In those predisposed by poor heredity or unstable constitution, the type of neurosis is determined by personality traits and previous mental health, and ordinarily conforms to the individual's usual pattern of reaction to stress. Exceptional stress such as exposure to intense enemy action may occasionally cause neurosis even in stable persons. When, therefore, a patient, who has recovered from an acute illness during war time, shows symptoms of a psychiatric disorder, what criteria should one use before attributing the neurosis to the infectious illness? If there is no known predisposition to neurosis or history of previous organic disease of the C.N.S., or of head injury, and if there is evidence of temporary cerebral disturbance during the acute illness, then in the absence of other discernible stress, the infection is probably responsible for the persistence of symptoms, or for the development of new symptoms during convalescence, when the cerebrospinal fluid has become normal.

Application of these criteria.—For the purpose of this study, patients were divided into three groups according to whether their previous personality was good, fairly good or neurotic. The first group consisted of well-organized and stable persons with friends, hobbies and interests, and with good work records. The second group consisted of timid and dependent persons with fair work record, while chronic neurotics with poor work records, hysterical persons, psychopaths and borderline mental defectives were included in the third group.

Pattern of symptoms in the organic group.—The individual symptoms did not differ essentially from those commonly seen among Service patients suffering from neurosis, but taken collectively, certain features were common to all the patients in this group, though

there was variation in their intensity. Mild, but persistent depression without self-reproach, frontal headaches, forgetfulness, and a pronounced tendency to invalidism was a syndrome frequently met with. All patients had varying degrees of changes in personality. Generally speaking, they seemed to have become timid, restricted in interests, dependent, lacking in self-confidence, and in consequence in their capacity for work. They seemed unable to settle down in their Units or after discharge from the Forces to their previous civilian occupations without craving for extra privileges from employers or work-mates. Forgetfulness appeared to be the result of intellectual deterioration which, in these patients, consisted in difficulty in calling up associations, poor learning ability, and in failure in tests of memory span for digits or sentences. Comprehension of new material was slow, and effortful. In learning anything new, they had to absorb it piecemeal, rather painfully and even when given directions, they could attend to only a limited amount at a time. Difficulty in recalling things which change constantly, such as dates, and time, and difficulty in forming new associations was present. For instance, although they read the daily newspapers and heard the radio, they had no knowledge of recent events in the theatre of war. Their so-called logical memory was also poor as they experienced difficulty in planning ahead quickly. While speaking to persons whom they knew, they could not recall their names. As more than one patient remarked, he "just couldn't get the name off the tip of his tongue". Although these patients showed no neurological signs of cerebral damage, the picture resembled clearly that of organic cases of known pathology.

Tables I and II show that neurotic symptoms were present where predisposition existed.

TABLE I.—NEURO-PSYCHIATRIC AFTER-EFFECTS OF CEREBROSPINAL FEVER.

Previous personality	Sex	Details of C.S.F. (D = Delirium)	No.	Other stress	Symptoms continuous	Type of disorder Neurosis	Probably organic
Good I	F.	Mild	1	1	—	1	—
	M.	Mild	4	1	3	4	—
	M.	Severe with D ...	6	—	6	2	4
	M.	Severe without D ...	3	—	3	3	—
Fairly good II	M.	Mild	2	1	2	2	—
	M.	Severe with D ...	3	3	3	2	1
	M.	Severe without D ...	2	—	1	2	—
Neurotic III	M.	Mild	6	4	5	6	—
	M.	Severe with D ...	3	3	3	1	2
	M.	Severe without D ...	2	—	2	2	—

TABLE II.—PRESENT SYMPTOMS.

(Symptoms common to three groups)

	Groups		
	I	II	III
Headaches	10	6	7
Depression	7	7	8
Forgetfulness and loss of memory ...	8	1	6
Change in personality	4	—	3
Disturbances of sleep	4	2	1
Irritability	5	—	1
Dizziness	3	—	3
Mild anxiety states	2	1	—
Effort syndrome	4	—	2
Fatigue	2	3	2
Deafness	1	1	—
Disorders of conduct	—	—	4
Sexual anomalies	—	2	3
Fainting fits	—	3	3
Enuresis	—	1	—
Vomiting	—	1	—
Hysterical:			
Motor	—	2	—
Sensory	—	1	2
Special senses	—	1	—
Visceral	—	1	3
Phobias	—	—	—

TABLE III.—FEATURES PRESENT IN 20 PATIENTS WHO HAD CEREBROSPINAL FEVER IN CHILDHOOD. SYMPTOMS DATE SINCE THEIR ILLNESS.

Previous neurotic traits ...	...	20	Hysterical:	
Backward at school ...	...	11	Motor	1
Fainting fits	...	7	Sensory	1
Periodic headaches ...	...	10	Visceral	—
Periodic depression ...	...	9	Dependent and timid personality	15
Difficulty in memorizing ...	...	8	Poor work record	16
Persistent somnambulism ...	...	4	Disorders of conduct	1
Avoidance of opposite sex ...	...	14	Phobias	6
Enuresis	...	3		

(Average age 23·6.)

Patients with present neurosis who had had cerebrospinal fever in childhood had shown backwardness at school, learning difficulties and later incompetence at work, and also dependency on parents. In view of the changes observed in adults, the early cerebrospinal fever was most probably a factor in such life-histories.

The methods of treatment were similar to those usually employed in psychiatric hospitals. Of 32 patients, only 3 remained on full duty, and 16 were invalided out. These 3 had only mild attacks of C.S.F. Out of 12 patients with history of delirium, 10 were invalided out, and of 7 patients with severe attacks without history of delirium, 3 were invalided out. None who had a severe attack returned to full duty. These figures indicate that the prognosis is worse than in other neurotic patients in the hospital.

The four undoubtedly organic cases were followed up, and it was found that the symptoms persisted, and their work record had been bad after discharge from the Army.

TABLE IV.—RESULTS OF TREATMENT

Group	Sex	Details of cerebrospinal fever		Re-covery	Much im-proved	Slightly im-proved	No improve-ment	Same R.T.U.	Light Cat. C.	Cat. E.	Follow-up
I	F.	Mild	1	1	—	—	—	1	—	—	
	M.	Mild	4	2	—	2	—	2	2	—	1 invalided 10 months later.
		Severe with D.	6	—	1	4	1	—	2	4	1 invalided 3 months later.
		Severe without D.	3	—	—	3	—	—	2	1	
II	M.	Mild	2	—	—	2	—	—	2	—	1 upgraded. 1 working efficiently and willingly 12 months later.
	M.	Severe with D....	3	—	—	2	1	—	1	2	
	M.	Severe without D.	2	—	—	1	1	—	1	1	—
III	M.	Mild	6	—	2	4	—	1	4	1	1 invalided from unit.
	M.	Severe with D....	3	—	—	2	1	—	1	2	1 relapsed 3 months later and was in another hospital.
	M.	Severe without D.	2	—	—	2	—	—	1	1	

D = Delirium.

CONCLUSIONS

That all those patients with subsequent organic syndrome had had a severe illness with delirium is suggestive, but not conclusive, as one deals here with highly selected material, and one does not know the number of patients who, after having had delirium, made complete recovery. In delirious patients, the disturbance of consciousness would indicate temporary alteration of cerebral function. When, therefore, after the acute phase, symptoms persist or there is deterioration, it would not be unreasonable to assume that permanent damage remains, or that recovery of function has been delayed.

Early occupational therapy as soon as possible after the acute phase, rehabilitation and adjustment to such limitations as exist, based on a consideration of patients' psychological and socio-economic problems would appear to be indicated in preventing some of the *functional* after-effects observed in these patients.

(1) 32 recent instances of neurotic and other psychotic symptoms occurring soon after cerebrospinal fever were studied.

(2) Four patients had developed an organic syndrome and 8 a neurotic syndrome, though no predisposition or psychological stress was known to exist. In addition there were 3 probable organic cases, where previous predisposition to neurotic or psychotic illness existed, and 9 neurotic patients, although predisposed, had not been exposed to any known psychological stress.

(3) The organic syndrome took the form of changes in personality and mood, with defects of memory and only occurred when the C.S.F. had been severe, and associated with marked changes in consciousness.

(4) The neurotic syndrome showed no obvious differences from cases in which C.S.F. had not been entered into the ætiology.

(5) In another group of 20 chronic neurotic patients, C.S.F. in childhood may have been an ætiological factor in later neurosis.

(6) The prognosis in the 32 patients studied was worse than in other neurotic patients in the hospital at the same time.

A New Form of Group Psychotherapy [*Abridged*]

By Lieutenant JOSHUA BIERER, R.A.M.C.

THIS paper reports an experiment with a new method of group therapy which combines (*a*) individual treatment, (*b*) group therapy, and (*c*) situational treatment. The experiment took the form of helping patients to run self-governed clubs, both in mental hospitals and in connexion with the out-patient departments of voluntary hospitals.

The clubs meet weekly and are run democratically by the patients themselves, with new officers elected every three months, so as to give as many members as possible the chance of responsibility and initiative. So that patients may feel that they themselves are in complete control, the doctors and assistants, though attending regularly, behave as ordinary members, and any suggestions they may make must be behind the scenes. Other members of the hospital staff attend the in-patients' clubs only by invitation from members, which helps patients to feel that they can give as well as receive. The out-patient clubs may be attended by anyone, whether patients or not, so long as they have been invited.

Three different kinds of club have been tried with success. One for acute and not deteriorated in-patients, of both sexes and all ages, suffering from schizophrenia, anxiety states, depression, neurasthenia or paranoia: this club has dancing, discussions, games, card drives, sports and rambles. A second club, for the more chronic and deteriorated in-patients, is run at present by ex-officers from the first club, but will soon have some of its own members on the committee: their programme is simpler, based on the need for movement and collective action, with simple games, community singing and dancing. The third type of club, for out-patients (with some former in-patients where desirable) is run as far as possible like any social club, but essential factors are (1) that to avoid all possible stigma, the premises have no connexion with the hospital, (2) that the psychotherapist, social worker or Sister from the out-patient department should attend regularly. This creates an essential link for shy new members and gives them confidence, as well as giving doctor and assistants a chance to watch the patients' social adjustment from week to week. These out-patient clubs can be self-supporting, as they cost very little to run. They certainly help discharged patients to continue the adjustment begun in hospital, and probably lessen the number of relapses. They are valuable adjuncts to out-patient treatment.

Various problems connected with the clubs may be mentioned, such as the difference between the relationship of the therapist to a group and his relationship to an individual patient; the question of conflicting transferences, where the therapist in charge of the club is not the patient's own doctor; the need for at least a semblance of freedom in the in-patient clubs; the problems of stigma, time and place in the out-patient clubs; the complications which *might* have arisen, but did not, from mixing the sexes. All these problems were in fact solved with very little difficulty.

These social clubs achieve results at three different levels: (*a*) Merely as institutions: in any club people tend to lose their shyness and develop their initiative, and in mental hospitals the very fact of having a club of their own helps patients to forget the restrictions by which their lives are otherwise surrounded; (*b*) as forums for different forms of group therapy, such as mass treatment (i.e. group suggestion), class treatment (lectures and discussions) and collective treatment (different forms of group analysis and group activity); (*c*) as an opportunity for the psychotherapist and his assistants to apply as unobtrusively as possible different forms of situational treatment. This is a new approach, which means "any individually directed impersonal measure, undertaken by the psychotherapist and his assistants with the aim of achieving a certain change in the patient, they having a full knowledge of the analytical background of that particular patient, while he himself is ignorant of it".

Among the situations and symptoms which have been ameliorated by the clubs are shyness and loneliness, inferiority feelings, including those due to physical defects, e.g. alopecia; sexual maladjustment, lack of incentive, inability to co-operate, claustrophobia and agoraphobia, parental domination, acute disappointment.

The following suggestions may be useful:

(a) In clubs run for mental hospital patients and ex-patients, an enthusiastic doctor, an understanding superintendent and adaptable assistants are essential.

(b) In clubs connected with out-patient departments the important factors are the personal bridge between the department and the club, and the realization that the club is only an adjunct to treatment and never treatment in itself.

(c) In all the clubs, only those psychotherapists and assistants who feel they possess the ability to run them successfully should attempt to do so. They should obtain some experience and training beforehand. Assistants might in future be called "group thera- pists": meanwhile some social workers could help in the out-patient clubs and some occupational therapists in the in-patient clubs.

Conclusion.—Not only are friendly relationships one function of human beings, but from a psychological point of view they are barometers of the state of health of each personality. A man without relationships not only feels the lack of them, but realizes that this lack is a sign of his failure in life. A lack of relationships is not the *cause* of mental illness, but merely a symptom. In curing that symptom, something much deeper is attacked. As the patient is assisted to make relationships, the proof of his failure is destroyed and a healthy personality begins to develop.

It is comparatively easy for the psychotherapist to solve conflicts, but much more difficult to restore self-confidence. The problem of group-psychotherapy is how to find a method which in a short time can produce good and lasting results, by a combination of *analysis* and *re-education.* The new approach just described aims at letting the patient *himself experience* situations which normally his deep conflicts prevent him from attempting. In this method, analysis follows rather than precedes the experience, and therefore the gulf between Insight and Realization is avoided.

Dr. E. B. Strauss: Freud has built up a system of psychology and psychopathology in terms of conflicts and tensions at the level of the sexual impulses; Adler has interpreted functional mental disorders in terms of disturbances at the level of the instinct of self-assertion. Is Bierer now about to start a system of psychology and psychopathology in terms of strains and stresses at the level of the herd- or community-instinct? Why not? Dr. Bierer has referred to society as an "entity" to which individual man is required to adjust. I would prefer to regard community as another "dimension", as it were, in which man, as a herd-animal, has to live and move and have his being. One thing is very certain, namely that if the group is a psychological entity, in the same sense in which an individual can be so regarded, the group is definitely inferior to the individual. It is important for an individual to be able to subordinate his own interests to the interests of the group, but there are great dangers associated with the *identification* of the indi- vidual psyche with the group-mind. One has only to think of Nazi Germany to realize the truth of that; moreover, the good effects of sudden religious conversions, brought about by emotional identifications with the group, are apt to be short-lived. Nothing can replace individual methods in psychotherapy. Dr. Bierer has complained of the mystery and magic with which the analytical psychotherapist surrounds himself, and has implied that it is used for its suggestive value. It must be pointed out that, until the completion of the psychodynamic interchange that occurs in analytical psychotherapy, it is undesirable for the analyst to become a flesh-and-blood figure; it is necessary for him to remain the blank screen, as it were, on to which the patient can project his hitherto-unconscious, emotionally toned imagery. That is an argument against a patient's psychotherapist being at the same time associated with the activities of the social club. I agree with Dr. Bierer that most psychotherapists, anyhow the good ones, are schizo- thyme rather than cyclothyme. But cyclothyme, extraverted qualities are needed for success in any form of group-psychotherapy. At the bottom of most psychological mal- adjustments there is the lack of a sense of *personal validity*; and any interests which restore this sense are acceptable. It seems to me that that is the most valuable contribution of social-club activities in combating mental disorders. The type of trouble that responds best to group methods is the condition that Kretschmer called "Sensitiver Beziehungs- wahn". Dr. Bierer mentioned a number of patients with paranoid characteristics who did well. One paraphrenic patient who failed to respond to analytical psychotherapy, on account of the violence of the negative transference, recovered as a result of group- therapy. Paranoid persons are unsuitable for analytical treatment precisely because of their inability to tackle the negative transference constructively. A negative transfer- ence is not an analytical accident which is to be avoided; on the contrary, it is a most valuable psychotherapeutic instrument.

Dr. T. P. Rees: We have had a club for patients known as "The Good Companions Club" running at Warlingham for the past four or five years. We find it an advantage to have a medical officer nominally in charge of all meetings, but no other members of the staff attend unless invited by the club. Approximately 10% of all the patients are members. Up to the present we have no experience of running a club for out-patients, but Dr. Bierer's paper should prove a valuable stimulus in that direction.

Another feature which we have found to be both popular and beneficial to the patients is a combined canteen and club room. This is open to all patients who enjoy ground parole which represents approximately two-thirds of the total population. The other patients have to be accompanied by a nurse. This club room is supplied with reading and writing materials and light refreshments are also served. It is open daily from 12 noon until 7 p.m., and later in the summer months.

I wonder to what extent the improvement noted by Dr. Bierer in his patients was due to the facilities provided for the free intermingling of the sexes. I am sure that the segregation of the sexes is at present being overdone in our mental hospitals.

JOINT MEETING OF THE SECTION OF PSYCHIATRY WITH THE MEDICO-LEGAL SOCIETY AT MANSON HOUSE, LONDON

Chairman—Roland Burrows, K.C., M.A., LL.D.

(President of Medico-Legal Society)

[*January* 27, 1944]

Criminal Responsibility and Medical Culpability [*Abstract*]

By W. Norwood East, M.D., F.R.C.P.

A criminal trial is a substitute for private war and, on occasions, must be fought with swords and not with foils. Unless this is clearly understood, the expert witness may allow calm scientific judgment to be ousted by emotion, and his evidence will lose some of its effectiveness.

Medical men do not usually censure the criteria required to establish a verdict that the accused is insane on arraignment. Their criticism, more often destructive than constructive, is reserved for the criteria of irresponsibility according to the McNaghten Rules. The McNaghten case never came before the House of Lords in its judicial capacity, and the well-known Questions of the Judges and the Answers of the Lords only referred to the effect of insane ignorance and insane delusions. But insanity affects the emotions and wills of men as well as their beliefs, and discussions concerning disorders in which emotional and volitional abnormalities predominate have brought about a wider immunity for insane persons than is sometimes supposed. In a recent trial for murder (R. *v.* Buckfield) the defence of an alibi failed, but the Judge when passing sentence of death informed the prisoner that "investigation would be made by the proper authorities as to whether there was any medical explanation of his act". And the Court of Criminal Appeal, when refusing to accept a plea of insanity which the jury has disregarded at the trial, frequently calls attention to the fact that the Secretary of State has special powers to enable him to order a medical enquiry concerning the mental condition of appellants convicted of murder.

Mercier, as the result of thirty years' close study, was unable to recall any case in which a prisoner was convicted on evidence that appeared to him to justify acquittal of the accused on the ground of insanity. For forty years I have been closely concerned with the subject, and have no doubt that the present procedure and practice result in justice being done to the public as well as to offenders. Zilboorg believes that the law relating to responsibility is unlikely to alter in the near future. Kinberg observes that, even if a serviceable definition of imputability could be made, it would be of no use, and would before long be a hindrance in the rational solution of problems connected with responsibility. I believe that if a medical formula of criminal responsibility was introduced we might be called upon to adhere rigidly to its specifications, with resulting hardship to offenders and embarrassment to psychiatrists. The urgent need of to-day is not a reform in the law regarding criminal responsibility, but an improvement in our evidence as forensic psychiatrists.

It seems that the principle of modified responsibility is accepted in cases of mental defectiveness, some cases of drunkenness and infanticide. The Mental Deficiency Act, 1913, provided alternatives to imprisonment. In D.P.P. *v.* Beard, the House of Lords established the principle that drunkenness not involving insanity might be a valid excuse in certain circumstances in negativing the fact that the accused had, at the time he did the act, the accompanying intent necessary to constitute the particular crime with which he is charged. The Infanticide Act, 1938, accepted the principle of a disturbed balance of mind, which in certain circumstances might justify a verdict of infanticide, and enable the defendant to be dealt with and punished as if she had been guilty of manslaughter and not murder.

The term *"criminal responsibility" is concerned with acquittal on the ground of insanity, and alternatively with conviction and punishment. I believe that psychiatry has advanced sufficiently to justify the acceptance of the principle of modified culpability in convicted offenders suffering from a recognized form of minor mental abnormality, if the degree of blameworthiness lies somewhere between that attached to the unlawful act of a normal person and one who is insane according to law. For this purpose a clear*

mental classification of offenders is necessary, separating the normal, subnormal, mentally defective, psychopathic personality, psychoneurotic and psychotic groups from one another. The mentally normal group of offenders is probably at least 80% of the receptions. Statistics show that the proportion of mentally defective is about 0·5% and of the insane 1%. Research is necessary before estimates can be made regarding the proportion of offenders who are subnormal, psychopathic personalities and psychoneurotics.

The normal group deserves close study as the term implies a hypothetical standard. It is misleading, and sometimes incorrect, to assess mental normality by normal conduct and successful social adaptation. If the view that normality is indefinable is accepted, diagnostic limitations and the necessity to estimate behaviour by the standards of others as well as one's own becomes apparent, and offenders in this group are seen to be responsible and culpable. There is no reason to consider that persons in the subnormal group are irresponsible, but there may be reason to believe, and occasionally to affirm, that their culpability from the medical point of view is lessened, particularly if they are known to be persistent offenders and their behaviour is unaffected by repeated sentences of imprisonment. Low-grade mentally defective persons if unfit to plead are declared insane on arraignment. Apart from the modified sentence passed upon others under the Mental Deficiency Act, 1913, medical opinion will usually agree that culpability may be lessened in some cases of high-grade defectiveness. The criminal psychopathic personalities include psychic inferiors, temperamentally unstable persons, alcoholists, drug addicts, true sexual perverts and non-progressive cycloid, schizoid and paranoid psychopathic personalities. In this group of non-insane non-sane deviates, the dividing line between abnormalities due to disease and anomalies of character is sometimes obscure. There is much to be said for the legal view that these offenders are responsible, but the nearer the condition is to mental disease and the further from an anomaly of character, the more inclined will be the observer to consider whether culpability should be modified. In the psychoneurotic and psychotic offenders responsibility according to law, modified degrees of culpability and of irresponsibility may be evaluated.

In cultured society the law must have the last word. But intensive study of the inherent mental constitution of offenders and the impacts of disease may enable medical evidence to assist a court to modify the award in a manner which will encourage social rehabilitation. Culpability, as I see it, is the more certain the more symptoms of recognized mental abnormality are lacking, the more insight the offender has into his condition, the more his emotional threshold is unaffected, and the more deliberately and frequently his will is concerned in the commission of the offence. The more satisfied we are that a crime is due to faults of character and not to the effects of disease, the more reason shall we have to consider that the law-breaker is responsible.

Mr. **Roland Burrows** (President of the Medico-Legal Society) said that the Society were very much indebted to Dr. Norwood East for his paper. It was always a good thing from time to time to examine general concepts to see whether they were really of as much value as they were habitually and unconsciously assumed to be. When a man of Dr. Norwood East's acknowledged pre-eminence discussed a topic of such importance as this they could not but be grateful to him for the light thrown not only on the conception but on the progress of information which enabled his hearers to determine whether their own concepts should be modified or not in the light of progress of knowledge.

With regard to criminal responsibility he spoke as a lawyer.

The underlying conception was that human beings must live in society. Society was only possible if its members lived according to rule, the rule constituted, in the ultimate analysis, something which would be enforced upon everybody by the whole of the individuals included in society. He meant "by the whole" substantially the whole. Of these rules some were what was known as the criminal law and as he understood them, crimes were supposed to be such acts so inconsistent with the life of society that their commission or omission would be punished—in other words, they must not happen. One tended to forget in dealing with the individual that the criminal law was established for the protection of the whole of society and when it came to a question of enforcing it one was up against certain facts which could not be ignored and which it was impossible to do without.

The rules of criminal law were difficult to establish and hard to alter and they tended therefore to lag behind contemporary opinion. That was why the offender sometimes

received a great deal of sympathy from people who were not minded to break the law. The administration of criminal justice was put into the hands of people who were getting older and whose concepts were based upon their past experience of twenty or thirty years ago and who tended, on the seat of justice, to be a little impervious to the views, ideas and experience of people who had come into existence at a later date. The topic was one which was simple in earlier times because if a person committed an offence of the kind known as a felony he was simply eliminated, but as the members forming society had increased so the importance of the ordinary individual who offended against the criminal law had become of more importance—or seemed to have done.

One had to remember when dealing with an individual who had offended against the law that he was a person who had shown by his actions that he had at least a tendency to be anti-social which, if it was allowed to grow, would tend to disrupt society altogether. Furthermore, on the conception of the criminal law that it resulted in punishment—a circumstance which is dominant although it is being modified very rapidly—a person who offended against the criminal law would, if simply punished, in the ideas of most people be unfairly treated and there had been evolved gradually a set of ideas which constituted the law relating to irresponsible persons, and assuming that that class of individual existed, and must exist, the conception of punishment in regard to such individuals became extremely difficult. If the simple idea of punishment was adhered to then it was unfair to punish. If the simple logic of the old common law was adopted, irresponsible people would go free and one would create a class of individuals like the *Herrenvolk* who were exempt from the law. It appeared to the speaker that if a person was to be treated as irresponsible on the ground of some peculiarity—to use a neutral term—then the corollary was that he should not be left free but should be put under some form of restraint.

Restraint was punishment however much one might object to it. What sort of restraint? This was where the medical profession came in. The lawyers could deal adequately with the bad man, but they were almost incapable of dealing with the mad man and they were certainly not capable of dealing with the treatment of the individual who was hovering between mad and bad. These were the individuals about whom Dr. Norwood East had been talking. It had been suggested, and it was a matter which required considerable thought, that the function of the criminal courts should be modified to a certain extent and he was not sure (although his mind was quite open on the subject) that there was not something to be said for it, that the function of the courts should be limited to saying whether the accused was guilty or not guilty of the offence charged. What happened to the defendant afterwards should be decided by some authority after proper consideration, and treatment, imprisonment or punishment imposed upon that individual so that he should if possible be turned into an ordinary law-abiding member of society or else excluded from society. That might or might not be combined with the discretion of the judge to determine whether it was a case where combined punishment or some form of precaution, such as probation, should be imposed, and limited only to those cases where, in the view of the court, a man should receive that kind of treatment.

Anybody like himself who was entrusted with the duty of sentencing people who had committed offences knew that the determination of the penalty was the most difficult and anxious part of the task of a criminal judge.

Dr. H. Crichton-Miller felt that Dr. Norwood East had left the impression that the present system could be adapted to the needs of real justice. He wondered if that was possible. The whole question of motivation had undergone a transformation in the last thirty or forty years and they were now faced with dealing with problems of culpability with unconscious motivation, perfectly clear to the psychiatrist but absolutely hidden from the public and the judiciary.

He would give an example; a woman was repeatedly arrested for shop-lifting, she was married to a town clerk and had two daughters. There was no cause for her shop-lifting, it was just absurd and on one occasion the magistrate said: "I must give this woman a lesson, she has been repeatedly convicted and a person of her social standing should know better", and he gave her a fairly round sentence. What were the facts known to the psychiatrist? She was very deaf and her deafness was incurable, and she was developing the paranoid system which so often accompanied progressive deafness. She had, however, another grievance even more biologically founded. She had always longed for a son but had been disappointed twice; she hoped for a son again but her husband said that there were to be no more children. Not only did he deny her maternal aspirations but he also refrained from satisfying her sexual desires. One saw perfectly well that but that woman could have been helped; one saw at the same time that she was not going to be helped by any lesson which the magistrate gave her. This was why the speaker

felt that they must go deeper than the question of public justice which left out, necessarily, considerations of that description.

Another example was that of a woman in her final year of medicine at a provincial University who had epileptic fits. One day in his waiting room she had the bad taste to undress and there was a minor domestic crisis in consequence. There was nothing to take her into the hands of the law but if she had come into the hands of the law, the question would have arisen as to whether she was responsible or not, and whether she was sane or insane. He would not like to think that a fifth year medical student was insane, some of the lawyers might have thought it was a possibility but he would assure them that it was not. The woman was wholly irresponsible and in the sense of the modern phrase this occurred while "the balance of her mind was disturbed". This was a good phrase and covered a good deal of suicides nowadays. But he was moved from that case to one who, more sane than the fifth year medical student, was a successful professional man and had many friends. He was popular and successful and had a 4-year-old son to whom he was devoted. He had a difference of opinion with his wife and she left him saying she was never coming back and that she was going to take his son with her. The man murdered the son and attempted suicide. That man was sane, that is, Broadmoor refused to describe him as insane, but for the purpose of the judiciary because he committed this act, he was a murderer and the verdict was "guilty but insane", therefore he was insane from the point of view of committing this act. He continued to spend his life in Broadmoor but he was not insane, that is to say, Broadmoor refused to give him any certificate of insanity which might allow of his estate being dealt with by others.

Could a clean cut be made on sanity or insanity? Surely the question of temperamentally irresponsible people must mean that there was a possibility of things happening which were not to be treated in the ordinary way.

Both psychiatrists and lawyers should make more clear the difference between the deterrent element in a sentence and the retributive, educational or rehabilitational aspects.

In such cases as shop-lifting he would have thought that a magistrate could differentiate in his sentence between so many days imprisonment as the minimal deterrent sentence for the act in question on the one hand, and, on the other, so many extra days as retributive or re-educative penalty for deliberate intention, or again no extra at all when unconscious motivation (and therefore irresponsibility) could be demonstrated. In other words, the deterrent factor in punishment must be maintained in the interests of society; the retributive must be adjusted to the degree of responsibility and attributed by the magistrate to the delinquent.

Lieutenant-Colonel J. D. W. Pearce, R.A.M.C.: As recently as 1937 Mr. Page said that a great majority of the general public, and indeed many judicial authorities, still regard with grave suspicion all medical evidence as to the mental abnormalities or psychological difficulties of a person charged with a criminal offence.

Criminal Courts are courts of law, not of morals, and the psychiatrist may well leave the problem of criminal responsibility to the lawyers and concentrate his attention on the concept of medical culpability. In this, however, he cannot exclude a consideration of moral law, nor can he fail to study the whole field of penology. Any major changes in law or judicial procedure should be based on really systematic psychiatric studies of antisocial conduct and antisocial persons. The aim of law and the aim of punishment are the protection of society. The reformation of the offender is an essential aim only in so far as it does not imperil society. For example, sexual offenders are by no means all amenable to treatment and on the question of culpability medical opinion is often at variance. It may be contrary to the welfare of society for a persistent sexual offender to be at liberty during the early stages of treatment. The need for society to be protected is exemplified in a case where the mother of a little girl 8 years old, having taken money from a middle-aged man, kept a lookout while he took the child into a wood and used her sexually. The unfortunate little girl subsequently became profoundly depressed. The analysis and explanation of such conduct surely make an urgent challenge to psychiatry.

I sometimes wonder how many doctors realize the immense toll of harm inflicted on society by the hard core of professional criminals. For a certain proportion of offenders the practical measure is permanent segregation, but society still baulks at this.

The real province for the psychiatrist is after the finding of guilt. It is then that psychiatric examination can best be carried out, and expert information submitted to the court to assist the court in reaching a wise decision in passing sentence. Only suitably trained and experienced doctors should be authorized to work in such an expert advisory capacity; otherwise a great deal of nonsense will be talked and published. Firmness and cruelty are no more synonymous than are mercy and weakness. Psychiatrists know that a really sharp punishment at the very outset of a delinquent career is frequently most

efficacious. It is the psychiatrist who is best equipped to assess the degree of real moral guilt in an offender. The study of medical culpability will establish finally that punishment based on expiation and retribution as well as rarely being effective is often frankly ill-advised; and that if it is to succeed in protecting society punishment must both be deterrent and reformative. I think, too, that in many indictable offences the principle of restitution is a wise one to apply. That very enlightened measure, the Criminal Justice Bill, provides opportunities for working out these problems of culpability. I think we have enough knowledge now to warrant active advocacy of a lowering or abolishing of the age-limit below which the principle of *doli incapax* applies. And such a law is surely mischievous which so ignores medical knowledge that it stipulates that a boy just short of his fourteenth birthday cannot have carnal knowledge; and which so disregards psychiatric knowledge as to say that he cannot have *mens rea*. We shall have much to say on this, a matter which might well be selected as one of the first problems demanding solution.

Dr. Norwood East, in reply, said that the time had not yet arrived to go deeply into medico-psychological explanations of crime because they had not only to retain as doctors the confidence of the lawyers and of the executive authorities but—a fact which nobody had mentioned—must remember that highly technical explanations of crime might antagonize the public. Unless the public were gradually educated into medical views a great deal more harm would be done to their cause than they might imagine. The lawyers and the executive authorities always gave doctors, wherever they could, their fullest confidence. Speaking from forty years' experience, he had no complaint to make either with regard to the lawyers or the executive authorities and he felt most strongly that doctors, by further close study of minor mental abnormalities, would better understand their cases and thus help the law. If the Criminal Justice Bill became law after the war a great deal of influence would be given to the medical profession to assist in the treatment and the deterrence of crime.

Section of Surgery

President—Sir JAMES WALTON, K.C.V.O., M.S.

[*December* 1, 1943]

DISCUSSION ON MODERN METHODS OF SKIN GRAFTING

Mr. Rainsford Mowlem : Ideal conditions for free skin graft are that the recipient area shall be recent, uninfected and vascular, and that the graft shall be maintained in close apposition to its bed for from five to ten days. In such circumstances failure can be due only to faulty technique.

Unfortunately in patients urgently requiring surgical epithelization the wounds are fibrotic, œdematous and infected, but the very unsuitability of the recipient area makes the problem more urgent. If the surface involvement is large the life of the patient may be jeopardized, and even in smaller areas persistent exposure and infection will result in continued fibrosis which ultimately freezes underlying muscles, tendons and joints into irreparable immobility.

Types of graft.—(*a*) *The split skin graft* is most commonly employed in varying thicknesses for the immediate repair of surgical wounds and for the epithelization of extensive skin losses. The oldest and still the commonest method of cutting these grafts is the freehand use of a Thiersch or a Blair knife, in conjunction with a board or suction box to create a steady plane.

A modification of the Blair knife consisting of the addition of a roller which admits only a predetermined thickness of skin does much to simplify its use although it imposes some limitations (Humby, 1936).

A more recent instrument is the Padgett dermatome (Padgett, 1939). In principle this is a half cylindrical drum carrying an oscillating knife edge; the drum, when coated with rubber solution, adheres to the skin, and the clearance between the knife and the drum can be prearranged to admit any desired thickness of skin. It must not be assumed that the graft so obtained has any new or specific characteristics except that it may be more even in thickness than that ordinarily obtained by freehand cutting. The apparatus does not eliminate difficulties, the chief of which is due to an uncontrollable factor, the rubber solution. This may result in imperfect adhesion to the skin so that no graft is cut or adhesion may be so firm that a thin graft cannot be removed from the drum without tearing. At the same time, the apparatus does allow the use of donor areas which would not otherwise be readily available, e.g. the skin of the abdomen, the back or the chest.

(*b*) *Whole thickness grafts* have two main indications: (i) In areas where colour and texture are important, e.g. on the face. (ii) Where freedom from secondary contracture is essential. e.g. the flexor aspects of the fingers and hand.

The methods of cutting are twofold, either by dissection with an ordinary scalpel or by a dermatome. Of these the former is more commonly used, chiefly because the graft must accurately fit the defect and is therefore usually irregular in outline. Whichever method of cutting is used, the resultant graft must be completely devoid of fat.

Pinch grafts have not been mentioned as their use results in extensive scarring of the donor area. Instead, a split skin graft cut either into small sections or into strips provides all the necessary mechanical advantages, whilst still leaving the donor area available for subsequent use.

Fixation.—All these grafts must be kept in close apposition with the recipient area for a period of two to ten days. This is usually carried out by pressure and the method of obtaining this is relatively standardized. It consists of:

(a) Suture of the margins of the graft to the recipient area. leaving one end of each stitch long. Handling of the graft at this stage may be facilitated by spreading it on tulle gras.

(b) The formation of a closely fitting mould of cotton-wool soaked in paraffin-flavine emulsion. The wool is built up in small pledgets to a thickness of about ½ in. and overlaps the area of the graft by about ¼ in. all round.

(c) Fixation of the mould by tying the long suture ends over it. The result is firstly to compress the mould on to the bed, and secondly to stretch the bed itself, so that the graft is sandwiched between two layers of force. The recipient area, the graft and the pressure pad are thus converted into one unit the various parts of which cannot move in relation one to another.

(d) The final application of pressure to the whole area by elastoplast, lastonet or crepe bandage (fig. 1).

Other methods of fixation are, of course, sometimes used, but the one described above is the most frequently applicable to surface areas.

PREPARATION OF THE RECIPIENT AREA

General.—There may be a danger of placing too much stress upon the types of surface application used and of ascribing to them too great a proportion of our success. These substances are only adjuvants which enable the patient to mobilize his immunity and reparative processes at the earliest moment, and attention must therefore be paid to the bearer of the raw area as well as to the area itself. Patients suffering from extensive granulating wounds apparently need more vitamin C than the normal patient. As much as from one to two thousand milligrams may be required to produce saturation, and though this state may never be necessary, the interrelationship between vitamin C and wound healing makes it obvious that attention to diet may be as important as the treatment of the wound. Many of these patients show a great tendency to dehydration, and others, particularly some months after their injury, present a gross degree of persistent anæmia. The former state will respond to good nursing, though the latter appears to be almost uncontrollable unless surgical epithelization is undertaken.

Local.—In recent surgical wounds only hæmostasis is necessary (fig. 2). In infected

FIG. 1.

FIG. 2.—Mr. John Barron's case. Avulsion of the scalp treated by immediate split skin graft. Note the transposed hairbearing flap to restore the anterior hair line.

wounds the problem is more complex. Until the advent of sulphanilamide and later penicillin, operation was often so long delayed that fibrosis in the depths of granulation tissue became sufficiently massive to cut off the surface blood supply. On such an area no graft could then survive and it became a practice to carry out a wide excision prior to grafting. 60% of a series of 140 cases reported by Rank (1940) were so treated and, as a result cellulitic invasion was by no means uncommon.

In 1941 the author published a short series in which infected areas had been treated by the application of sulphanilamide beneath the graft (Mowlem, 1941). The procedure, is as follows: Saline baths, 5% trypsin and the hypochlorites are used in the early separation of sloughs. Pressure, posture and sometimes active movements are employed against œdema. The sulphanilamide group is the chief weapon against infection and is always applied as an interval dressing even when other methods of treatment are in use. It is usually possible to render even an extensive burn ready for grafting in less than, thirty days (fig. 3). In this time there will be little deposition of deep fibrosis. At operation the granulating area is not disturbed but is dusted with sulphanilamide one-part, sulphathiazole three-parts immediately before the application of the graft. The sulphathiazole is employed on account of its slower absorption rate. All infected cases are bacteriologically controlled, and the streptococci occurring in the series here reported have been typed through the courtesy of Dr. S. D. Elliott. So far one sulphanilamide-

resistant strain has been encountered and fortunately only in one patient, for repeated grafts were uniformly unsatisfactory.

The other common organisms, *B. proteus* and *Ps. pyocyanea* are sensitive neither to sulphanilamide nor penicillin and though they seldom invade tissue they cause difficulty because of the amount of exudate they produce. This floats the graft away and can best be overcome by allowing exit space between strip or patch grafts. The appended

FIG. 3.—Full thickness burn of the thigh, shown above in the immediate pre-operative phase (5.10.42), and below in the healed state (22.12.42).

analysis of 535 grafts is made comparable with Rank's figures (1940) by taking the survival of 75% or more of the graft as an arbitrary criterion of success (*see* table).

GRAFTS SHOWING 75 PER CENT OR MORE OF PRIMARY "TAKE"

	Present series		Rank's series	
	Total	Successful	Total	Successful
Infected areas	279	221 = 79%	144	58 = 41%
Non-infected areas	256	240 = 94%	391	325 = 83%

It will be seen, therefore, that though there is a slight improvement in the results on non-infected areas, there is a much greater advance when grafting has been undertaken in the presence of infection. To-day the chances of successful grafting in the presence of infection have been almost doubled and operation has, on the whole, been undertaken very much earlier. This last point is of extreme importance as it confers the advantages of increased comfort and safety of the patient, of the diminution of damage from fibrosis and of the earlier commencement of full-scale reparative surgery.

The cases analysed above have been operated upon by a group of surgeons working in the Plastic Centre at Hill End Hospital. I am indebted to them for the use of their figures, and for their co-operation in this investigation.

REFERENCES

HUMBY, G. (1936) *Brit. med. J.* (ii), 1086.   RANK, B. K. (1940) *Brit. med. J.* (i), 846.
PADGETT, E. C. (1939) *Surg. Gynec. Obst.*, 69, 77.   MOWLEM, R. (1941) *Proc. R. Soc. Med.*, 34, 337.

PREPARATION OF THE RECIPIENT AREA

General.—There may be a danger of placing too much stress upon the types of surface application used and of ascribing to them too great a proportion of our success. These substances are only adjuvants which enable the patient to mobilize his immunity and reparative processes at the earliest moment, and attention must therefore be paid to the bearer of the raw area as well as to the area itself. Patients suffering from extensive granulating wounds apparently need more vitamin C than the normal patient. As much as from one to two thousand milligrams may be required to produce saturation, and though this state may never be necessary, the interrelationship between vitamin C and wound healing makes it obvious that attention to diet may be as important as the treatment of the wound. Many of these patients show a great tendency to dehydration, and others, particularly some months after their injury, present a gross degree of persistent anæmia. The former state will respond to good nursing, though the latter appears to be almost uncontrollable unless surgical epithelization is undertaken.

Local.—In recent surgical wounds only hæmostasis is necessary (fig. 2). In infected

FIG. 1.

FIG. 2.—Mr. John Barron's case. Avulsion of the scalp treated by immediate split skin graft. Note the transposed hairbearing flap to restore the anterior hair line.

wounds the problem is more complex. Until the advent of sulphanilamide and later penicillin, operation was often so long delayed that fibrosis in the depths of granulation tissue became sufficiently massive to cut off the surface blood supply. On such an area no graft could then survive and it became a practice to carry out a wide excision prior to grafting. 60% of a series of 140 cases reported by Rank (1940) were so treated and as a result cellulitic invasion was by no means uncommon.

In 1941 the author published a short series in which infected areas had been treated by the application of sulphanilamide beneath the graft (Mowlem, 1941). The procedure, is as follows: Saline baths, 5% trypsin and the hypochlorites are used in the early separation of sloughs. Pressure, posture and sometimes active movements are employed against œdema. The sulphanilamide group is the chief weapon against infection and is always applied as an interval dressing even when other methods of treatment are in use. It is usually possible to render even an extensive burn ready for grafting in less than thirty days (fig. 3). In this time there will be little deposition of deep fibrosis. At operation the granulating area is not disturbed but is dusted with sulphanilamide one-part, sulphathiazole three-parts immediately before the application of the graft. The sulphathiazole is employed on account of its slower absorption rate. All infected cases are bacteriologically controlled, and the streptococci occurring in the series here reported have been typed through the courtesy of Dr. S. D. Elliott. So far one sulphanilamide-

head skin or in some cases tubed pedicles from the chest. Furthermore, flaps are required for the repair of wounds of the extremities when the base of the defect is unsuitable for a free graft. If bone or tendon is exposed a full-thickness flap is essential and in the case of defects in the upper limb a direct flap from the abdomen is employed. Leg defects are usually repaired by a flap from the opposite calf.

Although flaps of various types are frequently used in late reconstructions there are very few indications for this method in the immediate treatment of facial or limb wounds. If a large area of the body surface has been denuded of skin a graft must be performed at the earliest opportunity, and it is now well established that a "skin dressing" applied within a few hours of the injury promotes rapid healing and a considerable reduction in the period of incapacity. In emergency surgery there are many factors which contra-indicate a flap repair. The general condition of the patient rarely permits a long anæsthetic, and the possibility of sepsis makes an extensive flap operation hazardous at this stage. As a general rule a free graft is used as immediate cover for any raw surface, and, if necessary, the graft can be replaced by a flap at a later date (*see illustration*).

Dr. A. H. T. Robb-Smith : Some experimental work was carried out by Mr. John Converse and myself on the healing of donor areas.

It seems remarkable that the use of donor areas for the experimental study of normal healing has been so neglected, and yet, apart from some histological observations by Brown and McDowell and the work of Cannon and Cope on the effect of various agents on the rate of epithelial regeneration, I can find no account of studies of this kind. In brief what we did was to take biopsies at varying intervals from the donor area of the same patient after a dermatome graft had been removed to aid the healing of burn wounds on other parts of the body.

In the first case a thin graft, 10/1,000 in. as measured on the section, was removed. Such a graft includes the whole of the epidermis and some of the superficial dermis, but the sebaceous glands and hair follicle roots are not included.

A biopsy, from the donor area two days later, shows a covering of blood clot and fibrin, a minimal cellular reaction in the dermis and epithelium beginning to grow out from the hair follicles. On the third day there is considerable extension of the epithelium over the bare dermis although not completely covered, and the epithelium is very thin and shows no keratinization. On the fifth day epithelization is complete and a little keratinization is present; further, the loose œdematous connective tissue which will form the new superficial dermis is appearing. On the ninth day the epithelium is quite thick, there is some formation of rete pegs and irregular epithelial downgrowths; the loose connective tissue of the new superficial dermis is clearly visible. The donor area at thirty-two days shows a normal undulating epidermis with melanoblasts and a collagenized superficial dermis.

Besides the regeneration of the nerve fibrils, melanoblasts and other elements of the dermis there is the regeneration of elastica which I believe to be all-important in the formation of a normal healthy flexible skin.

A section of the actual graft stained to show elastica shows a steady transition from the coarse, irregularly arranged fibres of the deep dermis to the fine vertical fibres of the superficial dermis. If the healed donor area is examined after twelve days, one finds that although the epidermis is satisfactory, yet no elastic fibres are present apart from those in the original donor area floor. By the thirty-second day the new superficial dermis is collagenized and fine vertical elastica fibres similar to those in the normal sub-epidermis are present.

It is well known that donor areas from which thick grafts have been removed heal slowly and often leave hard scars, sometimes keloidal, frequently covered with atrophic epithelium of poor quality; this slow healing is probably in large part due to the paucity of epithelial elements from which the regeneration may arise, as all the hair follicles and sebaceous glands may be removed in the graft, leaving only the ducts of the sweat glands to form epithelium; furthermore the epithelium regenerates more slowly from sweat ducts than from hair follicles and I believe that a slow epithelial regeneration causes a different type of dermis to develop which is an unsatisfactory support for the newly formed epidermis. This aspect of the problem is clearly of importance in the healing of burns and deserves further investigation.

Dr. P. H. Jayes : There are three methods of transplanting skin: (i) Free skin grafts; (ii) local flaps; (iii) flaps brought from a distance.

The advantages and disadvantages of using a free graft in preference to a local or distant flap must be carefully assessed. At present the free graft is employed for almost any repair without proper consideration for the cosmetic and functional result. Technical developments, such as the introduction of the Padgett dermatome and the Humby knife, have certainly increased the value and scope of the free graft, but there are still many defects which cannot be adequately repaired except by a full-thickness skin flap. The excellence of a flap repair cannot be appreciated until the skin has completely softened and settled into its new position. Flaps sometimes remain indurated and œdematous

Large loss of skin of right cheek. Thiersch graft applied immediately after the injury. Forehead flap six months later for cosmetic reasons. (Immediate graft performed by Mr. J. B. Cuthbert.)

for a considerable period after the operation, and unless these cases are followed up in six months or a year a false impression will be obtained as to the value of the method.

Free grafts will usually suffice for the repair of wounds in which the skin has been destroyed without loss of the deeper tissues. For defects of this type in the face local flaps, if available, are preferable as the skin will be of correct colour and texture whereas a graft tends to remain as a "patch".

When the loss involves the deep tissues a flap repair is indicated, as a free graft will not give *sufficient* restoration of contour. For example, a loss of the nose tip or a full thickness defect in the lips or cheek always necessitates a flap operation using the fore-
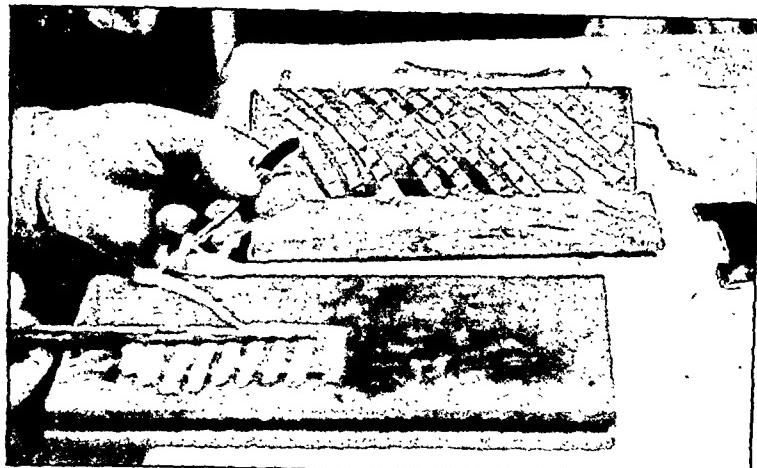
FIG. 1. — The squares on greasy paper ready to be grafted.

FIG. 2.—The grafts in position.

FIG. 4 (below). —A burnt thigh at the 10th day after the graft. Note the areas A and B corresponding to the diagram, p. 8.

Unfortunately it was not possible to obtain a complete series of biopsies from a donor area from which a thick dermatome graft had been taken.

In the second experiment a thick graft, measuring 50/1,000 in. on the section was taken (it should be emphasized that I have found no constant comparability between the thickness of grafts as estimated by the depth gauge of the dermatome and the actual measured thickness of the grafts when examined in the fixed and stained state). The complete hair follicles are included in the graft.

A biopsy taken on the third day shows little evidence of any epithelial formation whereas a superficial donor area showed considerable epithelization by this time. On the fifth day there is a slight epithelial outgrowth from the sweat ducts, the actual amount of epithelium formed being similar to that seen on the second day of a superficial donor area, but the total covering power is much less as the source points are so much more infrequent. By the fifth day the superficial donor area showed complete epithelization and the beginning of the new formed sub-epidermis which was absent from the deep donor area.

Unfortunately this experiment had to be terminated at this point but biopsies were obtained from another deep donor area in which healing was markedly delayed and the epithelium unsatisfactory.

In this case by the sixty-fifth day, epithelization is complete but the epithelium is thin without any rete peg formation or melanoblasts. It can be seen to have arisen from the sweat ducts and there is an enormous overgrowth of dermis which is 73/1,000 in. thick in contrast to a newly formed dermis of 14/1,000 in. in a healed superficial donor area. Furthermore there are bundles of horizontal collagen fibres of the type formed in keloids and it should be noted that these are not continuous but are separated at the points where the sweat ducts run up.

If one examines an elastica preparation one finds there has been no formation of elastic fibres in the new dermis, a consequential factor, associated, I believe, with the delayed healing and collagen overgrowth.

Dr. P. Gabarro : In this new method of skin grafting (Gabarro, 1943) I call these grafts *chess-board grafts* or *my squares*. McIndoe (1943) refers to them as *postage-stamp grafts*.

Technique.—(1) A graft of the desired thickness is cut from the donor area and spread over stiff sticky paper—I have been using the greasy paper supplied in the boxes of tulle gras. The raw side is left up. Paper and graft are then cut into strips of the desired width.

(2) These strips of skin with the paper are placed on another piece of the same paper, sometimes widely spaced, more frequently as close as possible and the whole is cut again, this time across.

The result is to obtain a strip of paper with skin grafts cut in squares, usually from ¼ in. to 1/10 in. in size. In this way they are easy to handle and can be evenly spread. Grafts and paper are placed on the raw area to be grafted (figs. 1 and 2).

The dressing.—The dressing is that of every graft. To fix the squares in position—which sometimes is not easy—long and narrow strips of tulle-gras are used, criss-crossing the grafted area. Often plaster of Paris is used for immobilization. The technique is not always the same. This depends largely on the case. In a few cases the grafts were left open to the air, without dressing.

The Fundamental Points of the Method

(*a*) Perimeter of the graft or possible growing epithelium : A square of skin with 2 in. sides has 8 in. of perimeter, but the same piece of skin cut in 64 squares—each one with ¼ in. sides—has 64 in. of perimeter. Therefore the smaller the squares the bigger is the perimeter of the grafts which is—in fact—the length of the possible growing epithelium.

(*b*) The drainage: If a continuous sheet of skin graft is used, it is not easy to provide good drainage for a possible discharge. *Any graft will take more easily in poor raw areas if there is enough room for discharge inside the whole area grafted.* No other type of graft provides better conditions for drainage than the individual small graft.

(*c*) Possibilities of the skin newly grown from the graft: These depend greatly on the local and general conditions of the patient. There are three different zones which we shall call A, B, C. A, the area of the actual graft which usually remains in excellent condition. B, an area all round the graft with good or fairly good skin. This is the skin grown in the three weeks following the grafting. C, a final area round B of epithelium grown later, with more or less fibrous reaction (fig. 3).

The ideal should be to put the grafts so close that the B skin will be able to bridge the gaps between the squares.

Evidence in support of this can be seen in the following case:

A patient[1] burnt by steam pouring for two and a half hours on his legs and arm was grafted on October 21, 1942, seven weeks after the accident. All grafts (120) took. At the tenth day the grafts had spread to four times their original size. The photograph taken at that date shows clearly the areas A and B (fig. 4). At the seventeenth day the whole area was covered by epithelium. A fragment of this grafted area was later sent for pathological examination to Dr. E. S. Smith of Manchester, who reported (referring to a previous case on which a dermatome graft had been used as a dressing): "There is much less surface desquamation in this section than in the other (the dermatome graft). The surface epithelium varies in thickness and has wavy contours. In some places it is possible to see the lines of junction of the grafts, but in others no definite line of demarcation can be seen. Coagulase material is less extensive than in the other specimen and the lymph channels are much nearer to the surface. There is also absence of the fibrous tissue noted in the other specimen."

(*d*) The donor area: In contrast with what happens in the pinch grafts, the donor area does not suffer at all and can be used again if necessary. The patient just mentioned had the graft cut twice from the left arm—the only limb available—and the same area could be used again if necessary.

(*e*) There is no contact between the recipient area and the donor area: This is sometimes very important. The graft to be cut in squares is always obtained before anything is done on the area to be grafted, and the donor area is already dressed when the graft is done.

(*f*) Time of the operation and number of squares: This technique enables an indefinite number of squares to be cut in a short time, and I have been able to graft and dress 200 squares in less than an hour.

RESULTS

These grafts have been applied to very different types of raw areas, on many occasions after the failure of other types of grafts. For experimental purposes they were applied on raw areas on which a "take" was not considered possible. The results in these last cases have been most encouraging.

CASE I.—This patient, twenty-five years ago had X-ray treatment for ringworm, and ten years ago developed necrosis of part of the right parietal area, and the pulsation of the brain could be seen. One-fifth of the ulcer was covered with my squares, and three weeks later the whole area was covered by thin epithelium. Six months later the thin epithelium was removed and a scalp flap was put on the resultant raw area. Some pus collected at the base of the flap, and a few days later the flap was necrosed at its distal part but some of the deep soft tissues remained adherent to the scalp. In this condition the skin in squares was grafted and spread all over the area in less than three weeks (figs. 5, 6 and 7).

CASE II.—Male, aged 55, was knocked down by a bus which caused a laceration of the leg about 11 in. by 5 in. in two zones: an upper one with very unhealthy-looking granulations and much discharge, and a lower one covered by necrosed tissue which at the operation was seen to be covering areas of slough. The operation was performed at this stage. All the sloughed tissues were removed, the granulations were shaved off and the squares were grafted. All took. A month later a complementary graft was done for very small areas remaining raw between the grafts and the result has been since then quite satisfactory (figs. 8 and 9).

CASE III.—Female, aged 62. Deep burn of the knee with necrosis and consequent infection. All the soft tissues in front and around the patella had to be removed together with the patella. The knee-joint was open and there was an abscess at one side. A split skin graft was cut in squares and placed all over the raw area, care being taken to leave well drained three clearly infected spots. All grafts took and joined together very well in a few days (figs. 10 and 11).

---

[1] This patient was presented at the Meeting of the Royal Society of Medicine.

FIG. 5.—(Case I).—A necrosed scalp flap on the right temporal (10.6.43).

FIG. 3.—Diagram showing the possibilities of the skin newly grown from a graft.

EPITHELIUM GROWN LATE

EPITHELIUM GROWN IN FEW DAYS

ORIGINAL SKIN GRAFT

A

B

C

VERY GOOD SKIN

FAIRLY GOOD SKIN or GOOD SKIN

SKIN WITH MORE OR LESS FIBROUS REACTION.
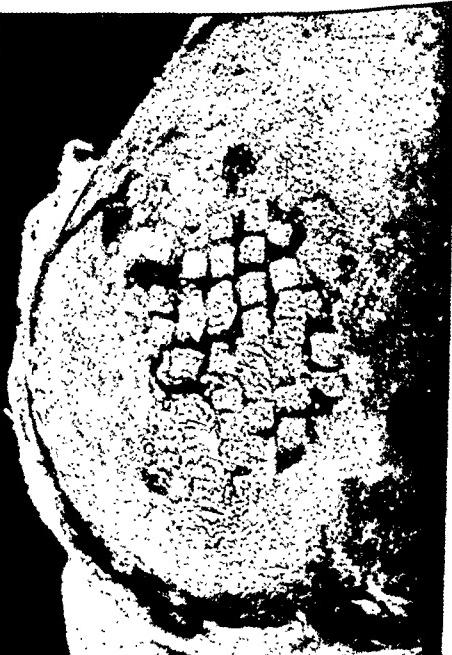
FIG. 4.—Diagram showing the possibilities of the skin newly grown from a graft.
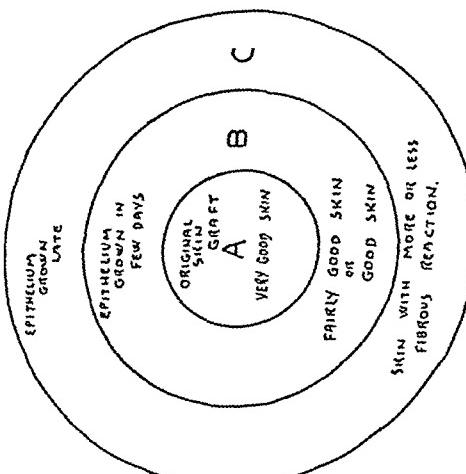
CASE IV.—Female, aged 56, had her scalp burnt in an epileptic fit in March 1942. Two months later the dead scalp was removed and multiple holes were made in the bone with the idea of stimulating the appearance of granulations, without success. I saw the patient in October 1942. In a first operation the outer part of the bone of the fronto-parietal region was removed down to the diploe. Fifteen days later the remaining bare bone was treated in the same way. There were already some granulations at the frontal part. 19 squares of skin graft were spread, 14 over the granulations and 5 on the newly cut bone (without much hope of success). Eight days later all grafts had taken including the 5 grafts on the bare bone. So, thirteen days later a graft 6 in. by 2½ in. was split in 100 squares and spread all over the granulations. Eleven days later practically all the granulations were covered by epithelium (figs. 12 and 13).

FIG. 12 (Case IV).—A burnt scalp with bare bone which has been perforated, unsuccessfully, to stimulate the appearance of granulations.

FIG. 13 (Case IV).—The same scalp treated by removal of the outer layer of the bone and Gabarro's grafts on the granulations. Five of the grafts took on the bare bone without granulations.

Comment.—Earl Padgett (1942) writes: "However, previous to the development of the dermatome occasionally a patient was seen in whom because of emaciation, long illness, the amount of raw area, or because of the technical impossibility of removing a sheet of skin from the area where the graft would necessarily have to be taken, small deep grafts were considered to be indicated."

Barsky (1938) wrote with reference to the pinch graft, considered up to now as the best small graft: "Their use is indicated only when it is not possible to obtain sufficient skin for a full thickness graft or a split-skin graft. There are several disadvantages attendant upon their use which are avoided by using another type of graft. The procedure itself is more time-consuming; the healing takes longer, since between these little islands there must be a new growth of epithelium."

Fomon (1939) says: "Many other methods of employing epithelium for grafting have been suggested but on the whole the results of this procedure have not been found sufficiently satisfactory to warrant their use."

In face of these opinions I propose to return to the original and most simple type of graft, using an improved technique.

The big sheet of Thiersch graft has many advantages when the possibilities of "taking" are good. A free graft of three-quarters of the skin and of even thickness provides the best possible result as a graft once it can be implanted on a healthy surface. Particularly in the face, there is nothing better than a flap, but I affirm that this type of small graft deserves an important place not only in plastic surgery but also in War surgery. It is very useful when large donor areas are not available. It takes more easily than the usual type of graft; its technique is simple and does not spoil the donor area. Although small, it takes well, grows easily, gets hold on areas apparently in bad condition, and gives fairly good skin, and sometimes very good skin.

REFERENCES

BARSKY, A. J. (1938) Plastic Surgery, Philadelphia and London.
FOMON, S. (1939) Surgery of Injury and Plastic Repair, Baltimore.
GABARRO, P. (1943) *Brit. med. J.* (i), 723.
McINDOE, A. H. (1943) *Proc. R. Soc. Med.*, 36, 647.
PADGETT, E. C. (1942) Skin Grafting, Springfield, Illinois.

FIG. 9 (Case II).—The same leg completely healed.

FIG. 11 (Case III).—The same knee completely healed.
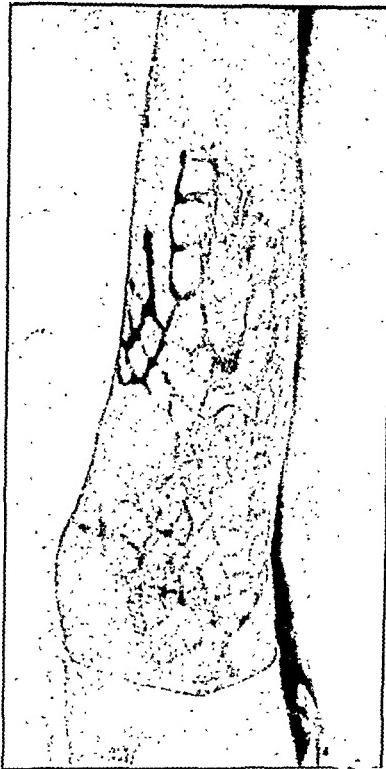
FIG. 8 (Case II).—A laceration of the leg with superficial necrotic tissue and much sloughed tissue underneath it. All was removed and grafted immediately.

FIG. 10 (Case III).—A knee with a deep burn and an abscess with all grafts taken.

uneventfully. At first the finger was stiff, but slight movement in the proximal inter-phalangeal joint was present after a couple of weeks and this has progressively improved.

Present condition.—The scar is soundly healed and linear, and there is no gross deep fibrous thickening. There is some tenderness due to nerve involvement at the proximal end of the scar. There is movement of only a few degrees at the distal interphalangeal joint, which is semiflexed. The proximal interphalangeal joint can be flexed freely and independently of the other fingers from the almost completely extended position to approximately a right angle. The function of the finger and of the hand is excellent (fig. 1).

Comment.—This case demonstrates that good interphalangeal movement and recovery of function may follow primary suture of a cut flexor tendon in its digital course. It has been asserted that such recovery never occurs, and most will be familiar with the pessimistic views expressed in the correspondence columns of the medical press a couple of years or so ago. Thus Coates (1941) stated, "the hopeless prognosis should be told to the patient and amputation considered"; an editorial (*Lancet,* 1941)
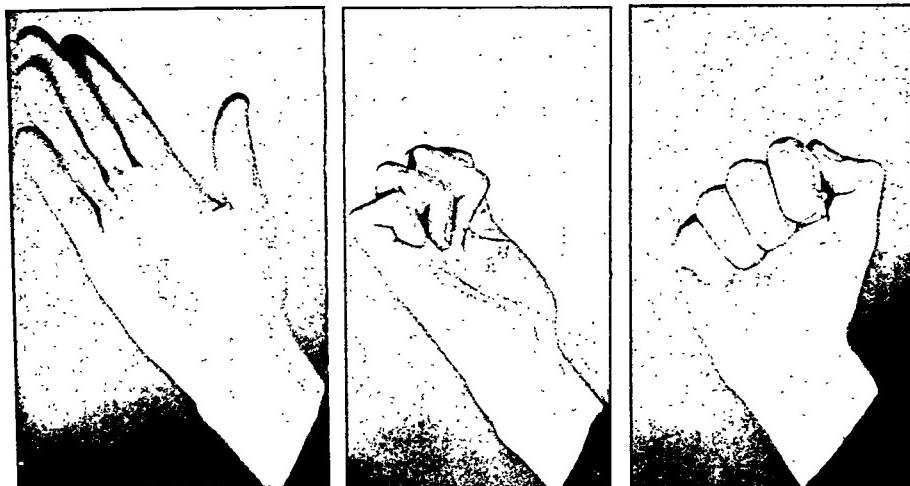
FIG. 2 (Mr. Eric Pearce Gould's case).—Showing result ten years after reattachment of flexor profundus tendon of ring finger right hand, the tendon having ruptured from its attachment subcutaneously.

sums up, "if the sheath is involved the prognosis is hopeless", and Yates (1941) con-cluded the discussion by the unanswered challenge: "Is there any surgeon in the land . . . who has succeeded in establishing a return of movement (active) in the interphalan-geal joints after any method of primary or secondary suture of flexor tendons within their digital sheath?" Iselin (1940) in the latest English edition of his classic work on the hand states: "I have personally never seen a good result following primary suture. I have, on many occasions and from numerous sources, been told of successes following primary suture. I have always made a point of going to examine these cases; they were all failures; they were fingers which were ankylosed in semiflexion by the operation scar, and which could be flexed *en masse* by the interossei at the metacarpophalangeal joint."

The only principle on which any substantial degree of success has been obtained up to the present has been that of avoiding tendon suture within the digital sheath altogether. Iselin's (1933) reinsertion operation and Sterling Bunnell's (1928) grafting operation are both based on this principle and both authors illustrate cases of active recovery of interphalangeal movement. That the principle is a sound one I have had the oppor-tunity of seeing for myself in a case on which I helped my former colleague, the late Mr. Eric Pearce Gould, to operate ten years ago. It was a case of subcutaneous detachment of the profundus tendon of the ring finger of the right hand from its attachment, the tendon being palpable, curled up at the level of the proximal phalanx. Mr. Gould opened the sheath over the proximal phalanx and pulled out the tendon, made another opening at the base of the distal phalanx, and by introducing a probe

[*January* 5, 1944]

The Effects of Rapid Decompression of the Bladder in Chronic Retention.—E. W. RICHES, M.S.

Male, aged 69, complained of increasing difficulty and frequency of micturition for six years; for one month past he had worn a urinal because of dribbling incontinence. Ten days before admission he was catheterized, about 30 oz. of clear urine being withdrawn. This was followed after a few days by hæmaturia which increased in amount and contained clots.

On admission.—The bladder was distended reaching above the umbilicus. *Per rectum*: Prostate enlarged. Blood urea 186 mg. per 100 c.c. The bladder was drained by a suprapubic catheter and decompressed slowly. Gross hæmaturia persisted and although the blood urea fell to 170 after two days and to 157 after five days hæmoglobin was only 28%. Blood transfusion (3 pints) was given by drip.

Cystoscopy on the fifth day showed blood clot at each orifice; when it was removed each efflux was seen to be bloody. Pyelography showed large hydro-ureters and hydronephroses. The urinary output began to fall on the fourth day after drainage, and signs of uræmia appeared on the sixth day. He died in uræmic coma on the eighth day after admission, eighteen days after catheterization. The blood urea was then 205 mg. per 100 c.c.

Specimen.—Shows distension of the bladder, ureters and kidneys, all of which are filled with blood clot.

A Case of Cut Flexor Tendons in a Finger Successfully Treated by Primary Suture.— D. H. PATEY, M.S.

Pilot Officer, Australian Air Force, aged 35. In April 1943 he severely lacerated the index finger of his left hand owing to the breaking of the porcelain knob of a door which was jammed and which he was trying to force open. He was admitted to hospital and operated on within a few hours. There was an irregular lacerated wound of the skin and subcutaneous tissues over the proximal and intermediate phalanges of the left index finger, the wound running down the ulnar side of the proximal phalanx
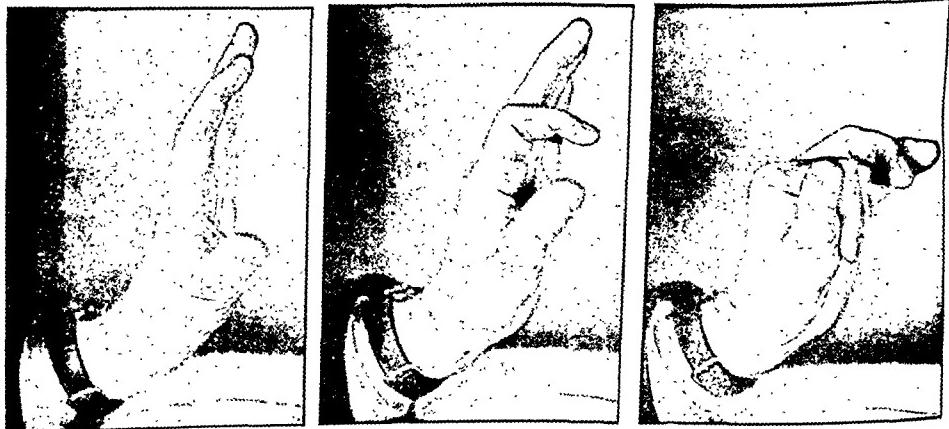
FIG. 1.—Showing range of movement in index finger of left hand following primary suture at level of proximal phalanx of cut flexor profundus tendon, the tendon sheath being excised at the same time and the flexor sublimis left unsutured.

and across the front of the intermediate phalanx. The fibrous flexor sheath was irregularly torn, and both flexor tendons were completely cut across at the level of the distal half of the proximal phalanx. A miniature débridement type of operation was performed, the minimal amount of skin edge being trimmed away together with some of the ragged subcutaneous fat, and a considerable part of the fibrous flexor sheath over the proximal phalanx being removed. The peripheral remains of the superficial flexor tendon were excised and its proximal end left free. The flexor profundus was joined by a Mayer-Bunnell stitch of medium stout silk. Sulphathiazole powder was dusted in the wound and the skin closed. The finger was fixed in plaster in semi-flexion for a week, and thereafter movements encouraged. The skin wound healed

18.10.43: Hepatic deflection colostomy (Devine) was done. Immediate improvement resulted and urine flow was from suprapubic wound and rectum in equal quantities. In fourteen days suprapubic wound was healed and after a further interval the colostomy was closed. Now passing urine and fæces *per rectum* without inconvenience.

II.—Mrs. M., aged 65. For five years had repeated cystoscopies and fulguration for papillomatosis of the bladder. The fulguration was done on two occasions through a suprapubic wound. In March 1943 carcinomatous change was diagnosed cystoscopically, the growth by this time had involved the internal meatus and caused retention of urine.

29.3.43: Bilateral implantation of ureters after one week's thorough sulphasuxidine therapy (continued for two weeks post-operatively). The left ureter was dilated probably from infiltration of the left ureteric orifice.

6.5.43: Whole bladder removed and as much of urethra as possible from above. Histological report (Prof. W. D. Newcomb): Alveolar and trabecular, transitional and polygonal-celled carcinoma of the bladder. Mitoses fairly frequent.

Recovery was smooth and urination *per rectum* has not been a great inconvenience.

The following cases and specimens were shown:

Extensive Fibrocystic Disease of Lower Jaw.—Mr. J. GABE.

Post-operative Result of Removal of Lower Jaw due to Fibrocystic Disease.—Mr. J. GABE.

Mediastinal Cyst. Successful Removal from Infant.—Mr. T. HOLMES SELLORS.

Pleuro-œsophageal Fistula Complicating Empyema.—Mr. T. HOLMES SELLORS.

Bilateral Lobectomy for Bronchiectasis.—Mr. T. HOLMES SELLORS.

Large Villous Adenoma of Rectum Removed by Combined Abdomino-perineal Excision.
    —Mr. E. C. B. BUTLER.

Argentaffinoma of Cæcum.—Mr. E. J. RADLEY SMITH.

Stress Fracture Through Site of Former Fracture.—Mr. E. J. RADLEY SMITH.

Bilateral Hypernephroma.—Mr. HOWARD G. HANLEY.

Jejunal Ulcer following Faulty Gastrectomy.—Sir JAMES WALTON.

[*February* 2, 1944]

Fatigue Fracture of the Tibia

By Surgeon Lieutenant-Commander K. J. O'CONNOR, R.N.

"FATIGUE" or "Stress" fracture of the tibia is a comparatively new clinical entity in this country. Dr. J. Blair Hartley of Manchester published a series of 14 cases in 1942, and I am indebted to him for most of my information on the subject. The following case recently occurred in a naval hospital. It demonstrates all the salient features of a "fatigue" or "stress" fracture. Much confusion has arisen due to the loose terminology. "Fatigue fracture" and "pseudo-fracture" are not, nor can they be, the same thing (Hartley, 1942, 1943). The term "pseudo" means "simulating" and the pseudo-fracture as found in Paget's disease and Looser's "Umbauzonen" is not a true fracture but only appears to be one radiologically. One point of differential diagnosis is the formation of callus: present in fatigue fracture and absent in pseudo-fracture.

J. R., an Ordinary Seaman, aged 18, was admitted to a naval hospital on 20.7.43 complaining of pain in the right leg about 3 in. below the knee for three weeks. He described it as a nagging ache which came on when he was standing and was relieved by rest in bed; there was no history of injury. He had joined the Navy four months before the onset of pain, and had done the normal training of a recruit. Just before entering hospital he had been undergoing an assault course.

He was a tall, slender, but healthy-looking young man, the only positive finding being a slight fullness below the right knee. Tenderness was absent and movements of the knee-joint full. X-rays, 22.7.43, showed "a lesion involving the posterior part of the right tibia about 3½ in. below the knee-joint; the anterior part of the bones was not affected. There was obvious periosteal proliferation both on the medial and lateral sides of the bone and on the posterior border . . . the films were suspicious of an osteogenic sarcoma" (fig. 1).

The Wassermann reaction was negative and the blood-count normal, and a biopsy showed only granulation tissue with a few osteoclasts.

A film taken on 2.9.43 showed a linear translucency entering the posterior aspect of the shaft of the tibia in the middle of the area of bony thickening running anteriorly for about two-thirds of an inch . . . "in appearance reminiscent of an incomplete fracture" (fig. 2).

A diagnosis was made of fatigue fracture and the limb immobilized in plaster until

from the distal to the proximal incision with the aid of a silk suture pulled the tendon down again in its sheath and reattached it. The perfect result at the present time is illustrated by the photographs shown (fig. 2).

The question arises of the reason for the degree of success obtained by primary suture in situ in the case I have shown. The only suggestion I can offer is that it was due to the excision of the fibrous flexor sheath during the course of débridement, so that there was no tendon sheath for the sutured tendon to become adherent to. As a result, the position was comparable to that of tendon suture in situations in which there is no fibrous tendon sheath, e.g. the flexor tendons in the hand or forearm, or the extensor tendons below the wrist.

Addendum.—During the course of the discussion, attention was drawn to an article by Mason (1940) advocating excision of the digital fibrous sheath. In the article Mason illustrates a case treated on these lines with a substantial degree of recovery of inter-phalangeal movement. The same principle has also been advocated by Jones (1941) and successful results claimed. If the validity of the principle of excision of the fibrous flexor sheath associated with suture of the tendon in situ is confirmed by further experience, it would seem to have the advantage of simplicity over the operative procedures of Iselin (1933), and of Sterling Bunnell.

REFERENCES

BUNNELL, STERLING (1928) *J. Bone Jt. Surg.*, 10, 1.
COATES, J. C. (1941) *Brit. med. J.* (i), 212.
ISELIN, M. (1933) Chirugie de la Main, Masson, Paris, 252.
—— (1940) Surgery of the Hand, London, 34.
JONES, R. M. (1941) *Lancet* (i), 492.
Lancet Editorial (1941) (i), 382.
MASON, M. L. (1940) *Surg. Gynec. Obstet*, 70, 392.
YATES, H. B. (1941) *Brit. med. J.* (i), 417.

Residual Ocular Palsies Following Cure of Myasthenia Gravis by Thymectomy.— A. DICKSON WRIGHT, M.S.

Female, aged 31. This was a severe case of myasthenia gravis of the localized type with the muscles of phonation so involved that without a recent dose of prostigmin she was quite unintelligible. Deglutition and mastication were only possible after injection of prostigmin, and suffocating attacks occurred from respiratory muscle involvement. Ocular palsies were impossible to analyse but were extensive and reading was quite impossible as were fixation and accommodation.

Total thymectomy was done after splitting the sternum from end to end and with the help of free prostigmin injections a good recovery was made.

Now residual paralysis of ocular muscles is disfiguring and disabling and the question of tendon transplants arises. Although phonation, mastication and deglutition are normal she takes one 15 mg. tablet of prostigmin every morning as she feels this makes her fit for the day's work. It is now eighteen months since the operation, and there are no signs of relapse, although it is important to note that in this case it took three months for recovery to take place after the operation.

Myasthenia Gravis Treated by Thymectomy.—A. DICKSON WRIGHT, M.S.

Nurse, aged 21. This was a case of severe myasthenia gravis of the generalized type. She was bedridden from the disease and taking more than 200 mg. of prostigmin daily. Thymectomy in two stages was done; there was practically no improvement after removing a large portion by the cervical route in July 1942. Complete thymectomy in September 1942 produced a dramatic result and within six weeks prostigmin reduction was commenced, and now she is symptom- and prostigmin-free and working in a munition factory.

Dr. Maurice Nellen has reported this case in greater detail recently (*Brit. med. J.*, 1943 (ii), 778).

Two Cases of Total Cystectomy for Carcinoma of Bladder.—A. DICKSON WRIGHT, M.S.

I.—W. S., male, aged 62. History of twelve months' frequency and hæmaturia with clots. The diagnosis of carcinoma was made on: (a) Large filling defect shown in excretion cystogram; (b) cystoscopic appearance: (c) consistency of tumour on rectal palpation.

23.9.43: Bilateral transplantation of ureters after thorough sulphasuxidine preparation. Recovery smooth.

11.10.43: Total cystectomy with prostate and vesicles. Histological report (Prof. W. D. Newcomb): Polygonal and transitional-celled carcinoma of the bladder. Mitoses numerous. Five days later, after removing drain from bladder bed, urine and fæces drained from the wound and patient's condition deteriorated.

ordered by the examining surgeon. An instruction card tied to the patient on admission helps to avoid confusion in the ordering of drugs, &c.

Adequate facilities for the giving of numerous transfusions must be available. In this incident most of the casualties came from the actual room where the bomb exploded and they were, therefore, very shocked. In all, 32 plasma transfusions were given, varying from 1 to 3 pints. No intravenous saline was used.

The value of pre-operative X-ray examination cannot be over-emphasized in all cases of retained foreign bodies, closed or compound fractures and chest injuries. The knowledge of the size, shape, and its course through the tissues is invaluable when planning the operation and the incision. I do not consider that accurate localization of F.B.s has any place in the emergency treatment; this is better done later. There is always plenty of time for the X-ray to be taken; very few cases require immediate operative treatment on admission and still fewer are in a fit state to receive it. No case should be taken to the theatre before adequate resuscitation which takes up to three or four hours. By following this rule we have only lost one post-operative case out of 150 and this was due to gas-gangrene on the fourth day.

Head injuries should be X-rayed as routine, even when there is no history of loss of consciousness. Again, some of the most severely shocked of our cases were found to have multiple or depressed fractures, other injuries being only minor.

The anæsthetist should play an important part in resuscitation; he can then accompany the surgeon on his round and help in assessing their condition and arrange the order of the operating list. To the anæsthetist can be left the ordering of any resuscitative measure during or after the operation. The anæsthetics of choice in our cases were gas oxygen and cyclopropane or ether. Intratracheal intubation was frequently necessary. Pentothal was only used in small doses (0·25 to 0·5 gm.) as an induction to very nervous patients.

Treatment of wounds with or without bony injuries consisted of careful débridement. This frequently necessitates opening up of tissue planes widely, and frosting of the tissues with sulphanilamide powder using an insufflator to prevent lump formation. Most wounds were left open or loosely sutured and drained with vaseline gauze. Compound fractures were put up in padded plasters after the minimum amount of manipulation had been carried out.

All burns were treated with sulphanilamide, in saline as a first-aid dressing; in the theatre after the burns had been thoroughly cleansed with ordinary soap and water followed by saline, they were frosted with powder and covered with tulle gras. This was then covered with wet saline packs, the moisture being kept in by a cellophane covering. As long as the dressing is kept damp there is no pain, the fingers or limb can be moved freely, while the patient, not apprehensive, co-operates readily. Full range of movement is regained even while healing is still taking place.

Another type of burn observed was thought to be due to a chemical irritant thrown out by the bomb. There was no evidence that this was a phosphorus compound. The burn was characterized by a dense black central scab with a small area of erythema around it with reaction extending deep into the subcutaneous tissues. The removal of the eschar made no difference to the fibrous reaction with which healing took place.

During the convalescent period a marked secondary anæmia frequently developed by the sixth or seventh day in patients who had not lost any quantity of blood and in some with no wounds at all. For this reason and also because of routine sulphanilamide therapy it is advisable to carry out frequent blood examinations. Iron and vitamin C should always be given orally.

J. E. H., aged 26. This patient was admitted unconscious and *in extremis*. At first, thought to be a head injury, he was later found to have the following: Concussion with cerebral œdema, ruptured abdominal wall through which just over 4 ft. of ileum had prolapsed and strangulated, also two large holes in the anterior and posterior walls of the cæcum. This was considered to be a blast injury to an abdominal wall weakened by a previous operation.

Although this patient did not regain consciousness his condition improved sufficiently in four hours for operation. The strangulated ileum was released by extending the abdominal wound; the two holes in the cæcum were closed by a double row of sutures. four feet of ileum had to be resected and an end-to-end anastomosis performed. The peritoneal cavity was drained by suprapubic stab wound. On return to the ward blood was given.

The patient regained consciousness three days later and was found to have cerebral irritation with a left-sided hemiparesis. On the tenth day his wound broke down forming a fæcal fistula. Two deep-seated abscesses had to be opened later and a further blood transfusion was given for persistent anæmia. His subsequent recovery has been uneventful; his mental condition has cleared up and his abdomen healed completely.

P. P., aged 15. Admitted with a wound 4 in. by 1½ in. in the left groin, heavily contaminated but not bleeding. X-ray showed a large metallic foreign body in the right thigh medial to the femur and below lesser trochanter. No bony injury.

7.10.43. Physiotherapy was then begun and convalescence was uneventful. A final X-ray 30.11.43 showed the bone rapidly resuming a normal appearance (fig. 3).

FIG. 1.—22.7.43.   FIG. 2.—2.9.43.   FIG. 3.—30.11.43.

Fatigue fracture of the tibia occurs usually in young men who have recently joined one of the Services. Fatigue fracture can be diagnosed on the history, clinical findings, and radiological findings.

History.—Pain in the affected leg, usually of sudden onset, coming on during exercise and relieved by rest. This is frequently noticed following a period of unaccustomed exercise. At first the patient may not consider the pain sufficient for him to seek the advice of his medical officer, and he only does so finally when he finds that continued exercise makes it worse. *There is no history of injury*, as this would obviously rule out fatigue fracture. Though one bone only may be affected the lesion can be bilateral but is never simultaneous.

Clinically, apart from slight swelling in the affected area nothing abnormal can be discovered. No other systemic disease is found in the patient.

The diagnosis can usually be made on repeated *radiological* examinations. There is subperiosteal proliferation increasing rapidly, usually on the concave surface of the bone—i.e. the "stressed" surface. Reference has already been made to the absence of this feature in "pseudo-fractures". This proliferation, with immobilization, shows steady organization. The fracture is frequently a fine "hair-line" running obliquely into the cortex, so fine that it is often missed. Usually the whole thickness of bone is not involved. It appears in the films very shortly after the onset of symptoms. The radiological appearance of the remainder of the bone is normal.

The order of frequency in the long bones is the metatarsals; upper end of the tibia; upper and lower ends of the femur and the fibula.

Pathological and pseudo-fracture occurring in diseases such as Paget's disease, osteomalacia and general systemic disease, are diagnosed on the general examination of the patient. Primary malignant disease of bone may in the early stage present difficulties, but will be diagnosed later radiologically or by biopsy. Further diagnosis must be made between fatigue fracture and osteitis due to infection, e.g. tuberculosis, syphilis, osteomyelitis, and simple fracture due to violence.

Treatment is rest, best obtained by immobilizing the limb in a weight-bearing plaster. Should the fracture have been missed and the diagnosis made only in the later stages when osteoporosis is considerable, excision of the area must be considered.

REFERENCES

HARTLEY, J. BLAIR (1942) *Brit. J. Surg.*, 30, 9; (1943) *Brit. J. Radiol.*, 16, 255.

Some Observations on Casualties in a Recent Air Raid

By Douglas Freebody, F.R.C.S.Ed.

The admissions during this raid were particularly heavy, 42 out of the 72 brought to hospital had to be admitted. The majority of these cases were severely shocked and threw a great strain on the resources for resuscitation. A pre-arranged routine of dealing with resuscitation was found invaluable; morphia, plasma or blood transfusions were

A plain radiograph of the limb showed a picture typical of that which Reichert claims to be pathognomonic of elephantiasis.

In view of the marked varicosities a Trendelenburg operation was performed. In doing this it was noticed that the subcutaneous tissues were myxœdematous in appearance, and that the superficial inguinal glands were neither larger nor more numerous than usual.

The patient was then discharged.

Three months later she was readmitted to hospital demanding amputation. There had been no relief from the tying of the saphenous vein and the limb was so cumbersome that she was unable to do her housework.

In view of the marked varicose veins the possibility of some underlying vascular disease was considered.

Mr. N. C. Lake performed an arteriogram on the right leg. The femoral vein was examined and found to be patent. The artery appeared perfectly normal. Pyelosil, 15 c.c., was injected into the artery; the radiograph showed no abnormality.

Accordingly, Mr. L. R. Broster amputated the limb just below the lesser trochanter. No difficulties were encountered although the two tourniquets method suggested by Bertwistle and Gregg (*loc. cit.*) was not adopted.

The ablated limb was dissected. All structures beneath the deep fascia appeared normal. The enlargement was entirely confined to the subcutaneous tissues. A section of the diseased area showed hyaline fibrosis and œdema of the dermis with slight infiltration by chronic inflammatory cells. Arterio- and veno-grams were carried out. the radiographs showing no abnormality. The vessels were subsequently dissected, no abnormality being detected.

She made a good recovery from the amputation and was sent home. Dr. Hegarty, of Luton, wrote to tell me that she had died ten weeks after the operation and that her death "was perfectly typical of pulmonary embolism".

Discussion.—The diagnosis of elephantiasis is made on the clinical examination together with the radiological and microscopic findings. The difficulty lies in the ætiology. The history is sufficient to exclude filarial infestation. In no way does this case resemble the disease described and named after Milroy (1892).

Although Hope and French (1908) described a case of Milroy's disease which went on to elephantiasis. the patient had suffered from repeated attacks of lymphangitis.

Illingworth (1939) states that congenital elephantiasis may not be obvious until later years. It is, therefore. suggested that this case was one of congenital elephantiasis.

The results of the dissection and arteriograms do not agree with the suggestion put forward by Gross (1914) that there is an underlying vascular disturbance in these cases. The occurrence of varicose veins is not unusual (Manson-Bahr, 1937).

The complete absence of inflammatory attacks and the proof of the patency of the vessels support the experimental work of Drinker (*loc. cit.*) that elephantiasis results from blockage of the lymphatics. the common occurrence of lymphangitis being purely incidental.

REFERENCES
BERTWISTLE, A. P., and GREGG, A. L. (1928) *Brit. J. Surg.*, **16**, 1, 62, 267.
DRINKER, C. K., FIELD, M. E., and HOMANS, J. (1934) *Amer. J. Physiol.*, **108**, 509.
GROSS (1914) *Dtsch. Z. Chir.*, **127**, 1.
HOPE, W. B., and FRENCH, H. (1908) *Guy's Hosp. Rep.*, **15**, 5.
ILLINGWORTH, C. F. W. (1939) A Short Textbook of Surgery, London, 131.
MANSON-BAHR, P. (1937) Post-Graduate Surgery, Ed. R. Maingot, London, Vol. III, 4210.
MILROY, R. W. (1892) *N.Y. med. J.*, **56**, 505.

Multiple Primary Carcinomata

By J. R. M. WHIGHAM, M.C., M.S.

HERE are four brief case extracts of patients, the unfortunate sufferers of what is presumably a second carcinoma. The subject is a perplexing one for even the seemingly clear case leaves an unsatisfactory feeling of doubt as to its true nature.

CASE I.—M. M., female, aged 69, operated on nine years previously for cancer of body of uterus. Now returned with blood in stool and loose masses also: auricular fibrillation also present. Perineal excision performed for cancer of rectum (2.8.41). Patient died three weeks after operation. The histology of the two growths was not unlike, both being a columnar-celled carcinoma. The rectal growth was the usual ulcerating growth with everted edges.

CASE II.—S. N., female, aged 74. A bilateral synchronous carcinoma of the breast, the left tumour of three years' duration, the right five days. There were no enlarged glands, or secondaries elsewhere in the body. At operation (29.12.42) the tumour on the right side was excised locally, and a biopsy performed on the left. Multiplicity in the breast is always open to criticism, the strong presumption being that the second growth is in fact a metastasis of the first. The following comment by Dr. Bratton, therefore. is of interest: "The tumour from the right breast gives one the idea that it may have arisen in a 'duct papilloma'. Though the tumours have grown in a different way, their cells are of exactly the same type, but this does not mean that they are not independent primaries" (*see Brit. J. Surg.*, 1944, 31, 303).

CASE III.—H. C., male, aged 63. Unable to pass water: suprapubic cystotomy performed: died four months after (27.8.43). Operated on five years previously for carcinoma cæcum.

At operation the track of the missile was found to have passed obliquely across the front of the pubis leaving a deep groove in the bone. The foreign body was removed through a second incision to the inner side of the right femoral vessels. After débridement both wounds were loosely sutured and drained.

The patient made very good progress until the third day when in spite of routine sulphanilamide, full therapeutic doses of anti-gas-gangrene serum and blood transfusion she developed a fulminating gas-gangrene infection and died the next day.

Amputation Under Ice Anæsthesia [*Abridged*]

By SOL M. COHEN, M.A., F.R.C.S.

A STUDY of mortality figures of amputations in the aged discloses a surprisingly high figure; for example, 59% in 120 cases at the City Hospital, New York, where the extremes of poor and derelict persons are received. To grasp at any method which gives promise of being able markedly to reduce this mortality in itself seems logical. Within recent years the importance of damping down, by the use of cold, the cell metabolism in the anæmic limb or arteriosclerotic leg has become generally recognized. The wider use of "icing" for the limb with arterial embolus, for "crushing" injury, in shock, indicated the need for trying out this apparently "safe painless" procedure. I have used the method on "poor risks" in 11 cases. The original technique of Allen of New York has been closely followed. A tourniquet is essential. Ice-bags are applied for twenty minutes before the icing starts, to the tourniquet site. After applying the tourniquet the entire limb, including an area 2 in. above the tourniquet, is packed with finely chipped ice and enclosed in rubber sheeting. Two and a half to three hours' icing is required for an amputation through the thigh. The method is not a freezing of the tissues; its purpose merely is to lower the temperature sufficiently to interfere with nerve conduction.

The icing is absolutely painless, none of the patients complain of the cold, and they are completely unaware of the tight tourniquet. Blood-pressure and pulse records during the icing stage and during the operation show that there is no shock, no after-pain, and subsequently no chest complications. Of the eleven cases, all except one had lower thigh amputations. Half the cases were over the age of 75; eight of the amputations were for arteriosclerotic gangrene, one for an old septic crushed foot, one for senile tuberculous knee-joint, one for gangrene following an arterial embolus. There were no immediate deaths, and complete analgesia was obtained, except in two, who had pain on sciatic nerve section (both cases had knee flexion contractures which interfered with adequate refrigeration of the back of the thigh). There were three late deaths—two were "institutional" deaths, one followed probably pulmonary embolus and is therefore directly connected with the operation. Delay in wound healing was a definite problem, and is a distinct disadvantage.

The method may be described as an interesting innovation and is of definite value in diabetic and arteriosclerotic gangrene.

The full text of this paper will be published later in the *Lancet*.

[For full references *see* ALLEN, F. M., and CROSSMAN, L. W. (1943), *Anesth. & Analges.*, 22, 264.]

Congenital Elephantiasis

By W. E. SPRINGFORD, F.R.C.S.

CASE REPORT

G. M. P., married, aged 37, was admitted to hospital complaining of pain in her right leg brought on by standing or walking.

Since the age of 10 her right leg had been swollen below the knee. Whether it was enlarged before this she was not prepared to state as it had caused her no trouble until recently. For at least the last three years the swelling had been present above the knee up to the groin. For the last twenty years she had noticed varicose veins in the limb which had not responded to injection treatment two years previously.

Past history.—Dermoid cyst removed from pelvis twelve years ago. Surgical sterilization seven years ago (her doctor informed me that no abnormality was reported in the pelvis). She had never been overseas.

On examination.—The right leg was enormous in size in comparison with the left. The swelling extended from the foot up to the groin, stopping sharply at this point. The skin was pale, cold and sweating profusely. The limb was more hairy than the other. Large and profuse varicose veins were present, in appearance like scattered grapes. The tissues felt brawny and did not pit on pressure except over the dorsum of the foot.

The function of the limb was limited solely by its weight.

When standing, the limb increased in girth, proved by measurement, and the patient became pale and breathless. Sitting in bed did not relieve the dyspnœa but immediate relief was obtained by elevating the limb. The patient then volunteered the information that she never dared to get up unless she first securely bandaged her leg.

JOINT DISCUSSION No. 1

Section of Physical Medicine with Section for the Study of Disease in Children

Chairman—P. BAUWENS, M.R.C.S., L.R.C.P.

(President of the Section of Physical Medicine)

[*November 17, 1943*]

DISCUSSION ON ANTERIOR POLIOMYELITIS

Major W. J. Stewart, U.S.A.M.C.: These are some impressions gained at first hand at the clinic where Sister Kenny's method of therapy was being used. About 60 acute cases were admitted to the Minneapolis General Hospital in a two-year period beginning in June 1940. These cases were checked by competent pædiatricians, orthopædists, and others. In addition, about 30 more cases were handled at the University of Minnesota Hospital. I visited the clinic with a group of physiotherapists and orthopædists; and for about eight months I visited there every few weeks and saw most of the cases and was able to observe their progress.

In addition, I saw most of the cases presented that had been treated at the Minneapolis General Hospital from 1937 to 1940 by the then standard methods at that institution. Thus the same surgeon directed the treatment of this disease by two different methods in the same hospital.

In Sister Kenny's type of therapy all cases received hot fomentations on admission. If there was massive muscular involvement, and particularly if the intercostal muscles were involved, the technicians carried out the hot-pack therapy practically continuously until definite improvement could be noted. In less severe cases, the fomentations were applied for the twelve daylight hours and discontinued at night.

The packs are wrung out of boiling water, very rapidly and are applied at once to the affected parts, then wrapped in a rubber or oilsilk covering and lastly wrapped in a dry blanket or bath-towel. The packs are applied so as to cover the involved extremities between joints, which in general are not immobilized. However, the patient subjected to such extensive hot packing is in effect quite thoroughly immobilized. Formal splinting is not carried out except to prevent foot drop.

This whole procedure is done rapidly. The packs remain in place for one hour. Records show that the temperature drops from approximately that of boiling water down to a few degrees above normal body heat after the first seven to ten minutes. Thus the patient is periodically subjected to several minutes of extremely high temperature, followed by a longer period of a slight elevation.

The hot fomentations are used as long as "muscle spasm" persists. As muscular tenderness disappears, passive and then active movements of extremities are started.

Considerably more attention is paid to muscular activity by Sister Kenny's technicians than by most physical therapy workers. This muscle training or re-education is the last portion of the Kenny treatment and takes up an indefinite period of weeks or even months. Many of the cases were still under treatment two years after the acute onset of the disease, technicians carrying out a daily regime of muscle re-education.

In the first 84 cases of acute poliomyelitis treated by Sister Kenny's method, not a single case of scoliosis had resulted, whereas in a smaller number of acute cases of my own I had six or seven of these complications.

At autopsy a cancer of the prostate and the rectum were found. This comment accompanies the histological report: "It is possible, but unlikely, that the carcinoma of the rectum was secondary to the cæcum removed five years before as they are alike histologically. The prostate is an independent primary and it would appear that the patient had three carcinomata."

CASE IV.—M. F., female, aged 44. Large cystic swelling left abdomen three weeks; and possible smaller one on right side. Bowels open. Nil on rectal examination. At operation (21.8.43) two ovarian cysts removed; also induration and thickening resembling ring carcinoma noticed in pelvic colon. Barium enema later confirmed this. It was three months (2.11.43) before patient was seen again, when she was suffering from abdominal swelling, flatulence and difficulty with bowels. She died without operation. The ovarian cysts were carcinomatous and the colon growth was a columnar-celled carcinoma with secondaries in the liver and lungs. In malignant ovarian tumours it is notoriously difficult to differentiate between multiplicity and metastases. Both ovaries were affected but the large size of the cyst might allow of its being regarded as "not metastatic" in origin. There was little doubt that the colon growth was a primary tumour. Another interesting fact was that the remains of a branchial pouch was found in the patient's neck and a small colloid adenoma in the thyroid, drawing attention to the possibility of a congenital dysplasia, a point that is sometimes emphasized in discussions on multiple primary growths.

Since Billroth's case in 1869 various criteria have been set up by which the dual nature of the growth can be judged: (1) A comparison of the macroscopic and microscopic appearances of both growths and their site in the body. (2) The presence of any other foci which would suggest metastases. (3) The time elapsed between the first growth and the appearance of the second growth. (4) The influence of surgical removal on the prognosis.

Warren and Gates (*Amer. J. Cancer*, 1932, 16, 1358) collected over 1,000 cases (1,259) in which they included a number of skin carcinomata and Mr. Norbury in his Presidential Address to the sub-Section of Proctology in 1930 dealt exhaustively with the subject (*Proc. R. Soc. Med.*, 24, 198). It is an interesting fact that not a single specimen was to be found in the Royal College of Surgeons' museum when a search was made in the same year (1930). It has also been suggested that these growths are so common that pathologists have ceased to collect them. In the published cases the incidence of multiple carcinomata in cancer patients is variously given, some high, some low, depending on the standard of criteria that has been satisfied, the figure being approximately 2 to 4%. Most are agreed that it is higher than can be explained by just chance. This suggests some ætiological factor. It is commoner in later life. Sex, apparently, is of no account. In some organs, the breast, the ovary, the uterus, the prostate, hormones may play a part. Congenital abnormalities and simple tumours are sometimes associated. Familial incidence is no higher than in single growths. It is unlikely that immunity is conferred by the presence of the first growth. There may even be an increased susceptibility but this has not been proved. Some multiple carcinomata have only been found accidentally at autopsies performed for other reasons, e.g. pneumonia, and probably more cases would be found if a complete microscopic examination could possibly be made as a routine.

Clinically the possibility of there being more than one lesion is of some importance to practising surgeons, from the point of view of both investigation and treatment, particularly when dealing with the digestive tract, where they are especially prone to occur. Multiple growths may be the explanation of unusual pain or a mystifying association of symptoms and if disappointment is to be avoided the possible existence of a second unsuspected primary growth, or indeed of several, must be borne in mind lest they be overlooked at operation.

[*March* 1, 1944]

MEETING HELD AT THE LONDON HOSPITAL

The following cases were shown:

(1) Foreign Body (clinical thermometer) in Stomach, Œsophagus and Duodenum, Removed at Operation. (With X-ray Films). (2) Thrombosis of Superior Vena Cava.—Mr. V. L. BILLINGTON.

Actinomycosis of the Appendix and Cæcum with Recurrent Psoas Abscess.—Mr. R. J. STEVEN.

(1) Obstructive Jaundice Following Cholecystectomy with Reconstruction of the Common Bile Duct. (2) Papilloma of Renal Pelvis with Hydronephrosis. Previous Operation of Division of Aberrant Renal Artery. (3) Enlarged Cervical Glands. ? Lymphosarcoma.—Mr. R. G. PARKER.

Fibrosarcoma of Tongue.—Mr. J. T. FATHI.

Osteogenesis Imperfecta Congenita.—Mr. J. SOUSTER.

Imperforate Anus and Recto-urethral Fistula with Operative Repair.—Mr. J. Y. MOORE.

JOINT DISCUSSION No. 1

Section of Physical Medicine with Section for the Study of Disease in Children

Chairman—P. BAUWENS, M.R.C.S., L.R.C.P.

(President of the Section of Physical Medicine)

[*November* 17, 1943]

DISCUSSION ON ANTERIOR POLIOMYELITIS

Major W. J. Stewart, U.S.A.M.C.: These are some impressions gained at first hand at the clinic where Sister Kenny's method of therapy was being used. About 60 acute cases were admitted to the Minneapolis General Hospital in a two-year period beginning in June 1940. These cases were checked by competent pædiatricians, orthopædists, and others. In addition, about 30 more cases were handled at the University of Minnesota Hospital. I visited the clinic with a group of physiotherapists and orthopædists; and for about eight months I visited there every few weeks and saw most of the cases and was able to observe their progress.

In addition, I saw most of the cases presented that had been treated at the Minneapolis General Hospital from 1937 to 1940 by the then standard methods at that institution. Thus the same surgeon directed the treatment of this disease by two different methods in the same hospital.

In Sister Kenny's type of therapy all cases received hot fomentations on admission. If there was massive muscular involvement, and particularly if the intercostal muscles were involved, the technicians carried out the hot-pack therapy practically continuously until definite improvement could be noted. In less severe cases, the fomentations were applied for the twelve daylight hours and discontinued at night.

The packs are wrung out of boiling water, very rapidly and are applied at once to the affected parts, then wrapped in a rubber or oilsilk covering and lastly wrapped in a dry blanket or bath-towel. The packs are applied so as to cover the involved extremities between joints, which in general are not immobilized. However, the patient subjected to such extensive hot packing is in effect quite thoroughly immobilized. Formal splinting is not carried out except to prevent foot drop.

This whole procedure is done rapidly. The packs remain in place for one hour. Records show that the temperature drops from approximately that of boiling water down to a few degrees above normal body heat after the first seven to ten minutes. Thus the patient is periodically subjected to several minutes of extremely high temperature, followed by a longer period of a slight elevation.

The hot fomentations are used as long as "muscle spasm" persists. As muscular tenderness disappears, passive and then active movements of extremities are started.

Considerably more attention is paid to muscular activity by Sister Kenny's technicians than by most physical therapy workers. This muscle training or re-education is the last portion of the Kenny treatment and takes up an indefinite period of weeks or even months. Many of the cases were still under treatment two years after the acute onset of the disease, technicians carrying out a daily regime of muscle re-education.

In the first 84 cases of acute poliomyelitis treated by Sister Kenny's method, not a single case of scoliosis had resulted, whereas in a smaller number of acute cases of my own I had six or seven of these complications.

At autopsy a cancer of the prostate and the rectum were found. This comment accompanies the histological report: "It is possible, but unlikely, that the carcinoma of the rectum was secondary to the cæcum removed five years before as they are alike histologically. The prostate is an independent primary and it would appear that the patient had three carcinomata."

CASE IV.—M. F., female, aged 44. Large cystic swelling left abdomen three weeks; and possible smaller one on right side. Bowels open. Nil on rectal examination. At operation (21.8.43) two ovarian cysts removed; also induration and thickening resembling ring carcinoma noticed in pelvic colon. Barium enema later confirmed this. It was three months (2.11.43) before patient was seen again, when she was suffering from abdominal swelling, flatulence and difficulty with bowels. She died without operation. The ovarian cysts were carcinomatous and the colon growth was a columnar-celled carcinoma with secondaries in the liver and lungs. In malignant ovarian tumours it is notoriously difficult to differentiate between multiplicity and metastases. Both ovaries were affected but the large size of the cyst might allow of its being regarded as "not metastatic" in origin. There was little doubt that the colon growth was a primary tumour. Another interesting fact was that the remains of a branchial pouch was found in the patient's neck and a small colloid adenoma in the thyroid, drawing attention to the possibility of a congenital dysplasia, a point that is sometimes emphasized in discussions on multiple primary growths.

Since Billroth's case in 1869 various criteria have been set up by which the dual nature of the growth can be judged: (1) A comparison of the macroscopic and microscopic appearances of both growths and their site in the body. (2) The presence of any other foci which would suggest metastases. (3) The time elapsed between the first growth and the appearance of the second growth. (4) The influence of surgical removal on the prognosis.

Warren and Gates (*Amer. J. Cancer*, 1932, 16, 1358) collected over 1,000 cases (1.259) in which they included a number of skin carcinomata and Mr. Norbury in his Presidential Address to the sub-Section of Proctology in 1930 dealt exhaustively with the subject (*Proc. R. Soc. Med.*, 24, 198). It is an interesting fact that not a single specimen was to be found in the Royal College of Surgeons' museum when a search was made in the same year (1930). It has also been suggested that these growths are so common that pathologists have ceased to collect them. In the published cases the incidence of multiple carcinomata in cancer patients is variously given, some high, some low, depending on the standard of criteria that has been satisfied, the figure being approximately 2 to 4%. Most are agreed that it is higher than can be explained by just chance. This suggests some ætiological factor. It is commoner in later life. Sex, apparently, is of no account. In some organs, the breast, the ovary, the uterus, the prostate, hormones may play a part. Congenital abnormalities and simple tumours are sometimes associated. Familial incidence is no higher than in single growths. It is unlikely that immunity is conferred by the presence of the first growth. There may even be an increased susceptibility but this has not been proved. Some multiple carcinomata have only been found accidentally at autopsies performed for other reasons, e.g. pneumonia, and probably more cases would be found if a complete microscopic examination could possibly be made as a routine.

Clinically the possibility of there being more than one lesion is of some importance to practising surgeons, from the point of view of both investigation and treatment, particularly when dealing with the digestive tract, where they are especially prone to occur. Multiple growths may be the explanation of unusual pain or a mystifying association of symptoms and if disappointment is to be avoided the possible existence of a second unsuspected primary growth, or indeed of several, must be borne in mind lest they be overlooked at operation.

[*March* 1, 1944]

MEETING HELD AT THE LONDON HOSPITAL

The following cases were shown:

(1) Foreign Body (clinical thermometer) in Stomach, Œsophagus and Duodenum, Removed at Operation. (With X-ray Films). (2) Thrombosis of Superior Vena Cava. —Mr. V. L. BILLINGTON.

Actinomycosis of the Appendix and Cæcum with Recurrent Psoas Abscess.—Mr. R. J. STEVEN.

(1) Obstructive Jaundice Following Cholecystectomy with Reconstruction of the Common Bile Duct. (2) Papilloma of Renal Pelvis with Hydronephrosis. Previous Operation of Division of Aberrant Renal Artery. (3) Enlarged Cervical Glands. ? Lymphosarcoma.—Mr. R. G. PARKER.

Fibrosarcoma of Tongue.—Mr. J. T. FATHI.

Osteogenesis Imperfecta Congenita.—Mr. J. SOUSTER.

Imperforate Anus and Recto-urethral Fistula with Operative Repair.—Mr. J. Y. MOORE.

JOINT DISCUSSION No. 1

Section of Physical Medicine with Section for the Study of Disease in Children

Chairman—P. BAUWENS, M.R.C.S., L.R.C.P.

(*President of the Section of Physical Medicine*)

[*November* 17, 1943]

DISCUSSION ON ANTERIOR POLIOMYELITIS

Major W. J. Stewart, U.S.A.M.C.: These are some impressions gained at first hand at the clinic where Sister Kenny's method of therapy was being used. About 60 acute cases were admitted to the Minneapolis General Hospital in a two-year period beginning in June 1940. These cases were checked by competent pædiatricians, orthopædists, and others. In addition, about 30 more cases were handled at the University of Minnesota Hospital. I visited the clinic with a group of physiotherapists and orthopædists; and for about eight months I visited there every few weeks and saw most of the cases and was able to observe their progress.

In addition, I saw most of the cases presented that had been treated at the Minneapolis General Hospital from 1937 to 1940 by the then standard methods at that institution. Thus the same surgeon directed the treatment of this disease by two different methods in the same hospital.

In Sister Kenny's type of therapy all cases received hot fomentations on admission. If there was massive muscular involvement, and particularly if the intercostal muscles were involved, the technicians carried out the hot-pack therapy practically continuously until definite improvement could be noted. In less severe cases, the fomentations were applied for the twelve daylight hours and discontinued at night.

The packs are wrung out of boiling water, very rapidly and are applied at once to the affected parts, then wrapped in a rubber or oilsilk covering and lastly wrapped in a dry blanket or bath-towel. The packs are applied so as to cover the involved extremities between joints, which in general are not immobilized. However, the patient subjected to such extensive hot packing is in effect quite thoroughly immobilized. Formal splinting is not carried out except to prevent foot drop.

This whole procedure is done rapidly. The packs remain in place for one hour. Records show that the temperature drops from approximately that of boiling water down to a few degrees above normal body heat after the first seven to ten minutes. Thus the patient is periodically subjected to several minutes of extremely high temperature, followed by a longer period of a slight elevation.

The hot fomentations are used as long as "muscle spasm" persists. As muscular tenderness disappears, passive and then active movements of extremities are started.

Considerably more attention is paid to muscular activity by Sister Kenny's technicians than by most physical therapy workers. This muscle training or re-education is the last portion of the Kenny treatment and takes up an indefinite period of weeks or even months. Many of the cases were still under treatment two years after the acute onset of the disease, technicians carrying out a daily regime of muscle re-education.

In the first 84 cases of acute poliomyelitis treated by Sister Kenny's method, not a single case of scoliosis had resulted, whereas in a smaller number of acute cases of my own I had six or seven of these complications.

At autopsy a cancer of the prostate and the rectum were found. This comment accompanies the histological report: "It is possible, but unlikely, that the carcinoma of the rectum was secondary to the cæcum removed five years before as they are alike histologically. The prostate is an independent primary and it would appear that the patient had three carcinomata."

CASE IV.—M. F., female, aged 44. Large cystic swelling left abdomen three weeks; and possible smaller one on right side. Bowels open. Nil on rectal examination. At operation (21.8.43) two ovarian cysts removed; also induration and thickening resembling ring carcinoma noticed in pelvic colon. Barium enema later confirmed this. It was three months (2.11.43) before patient was seen again, when she was suffering from abdominal swelling, flatulence and difficulty with bowels. She died without operation. The ovarian cysts were carcinomatous and the colon growth was a columnar-celled carcinoma with secondaries in the liver and lungs. In malignant ovarian tumours it is notoriously difficult to differentiate between multiplicity and metastases. Both ovaries were affected but the large size of the cyst might allow of its being regarded as "not metastatic" in origin. There was little doubt that the colon growth was a primary tumour. Another interesting fact was that the remains of a branchial pouch was found in the patient's neck and a small colloid adenoma in the thyroid, drawing attention to the possibility of a congenital dysplasia, a point that is sometimes emphasized in discussions on multiple primary growths.

Since Billroth's case in 1869 various criteria have been set up by which the dual nature of the growth can be judged: (1) A comparison of the macroscopic and microscopic appearances of both growths and their site in the body. (2) The presence of any other foci which would suggest metastases. (3) The time elapsed between the first growth and the appearance of the second growth. (4) The influence of surgical removal on the prognosis.

Warren and Gates (*Amer. J. Cancer*, 1932, 16, 1358) collected over 1,000 cases (1,259) in which they included a number of skin carcinomata and Mr. Norbury in his Presidential Address to the sub-Section of Proctology in 1930 dealt exhaustively with the subject (*Proc. R. Soc. Med.*, 24, 198). It is an interesting fact that not a single specimen was to be found in the Royal College of Surgeons' museum when a search was made in the same year (1930). It has also been suggested that these growths are so common that pathologists have ceased to collect them. In the published cases the incidence of multiple carcinomata in cancer patients is variously given, some high, some low, depending on the standard of criteria that has been satisfied, the figure being approximately 2 to 4%. Most are agreed that it is higher than can be explained by just chance. This suggests some ætiological factor. It is commoner in later life. Sex, apparently, is of no account. In some organs, the breast, the ovary, the uterus, the prostate, hormones may play a part. Congenital abnormalities and simple tumours are sometimes associated. Familial incidence is no higher than in single growths. It is unlikely that immunity is conferred by the presence of the first growth. There may even be an increased susceptibility but this has not been proved. Some multiple carcinomata have only been found accidentally at autopsies performed for other reasons, e.g. pneumonia, and probably more cases would be found if a complete microscopic examination could possibly be made as a routine.

Clinically the possibility of there being more than one lesion is of some importance to practising surgeons, from the point of view of both investigation and treatment, particularly when dealing with the digestive tract, where they are especially prone to occur. Multiple growths may be the explanation of unusual pain or a mystifying association of symptoms and if disappointment is to be avoided the possible existence of a second unsuspected primary growth, or indeed of several, must be borne in mind lest they be overlooked at operation.

[*March* 1, 1944]

MEETING HELD AT THE LONDON HOSPITAL

The following cases were shown:

(1) Foreign Body (clinical thermometer) in Stomach, Œsophagus and Duodenum, Removed at Operation. (With X-ray Films). (2) Thrombosis of Superior Vena Cava. —Mr. V. L. BILLINGTON.

Actinomycosis of the Appendix and Cæcum with Recurrent Psoas Abscess.—Mr. R. J. STEVEN.

(1) Obstructive Jaundice Following Cholecystectomy with Reconstruction of the Common Bile Duct. (2) Papilloma of Renal Pelvis with Hydronephrosis. Previous Operation of Division of Aberrant Renal Artery. (3) Enlarged Cervical Glands. ? Lymphosarcoma.—Mr. R. G. PARKER.

Fibrosarcoma of Tongue.—Mr. J. T. FATHI.

Osteogenesis Imperfecta Congenita.—Mr. J. SOUSTER.

Imperforate Anus and Recto-urethral Fistula with Operative Repair.—Mr. J. Y. MOORE.

The unit consists of three wards of 18 patients each and a treatment room with a team of workers comprising the medical staff, 7 physiotherapists, sisters, nurses and a porter; all of whom except the medical staff work full time on a treatment which is continuous every day of the week including Sunday.

On admission as early as possible after the onset of the disease a preliminary examination and discussion of the patient is undertaken by this team together to determine: (1) Extent of paralysis and the charting of muscle power; (2) the course of future treatment; (3) the method of maintaining position in bed.

Thereafter a general examination is made at frequent intervals, special care being taken to maintain good health and freedom from intercurrent infection, which seriously interferes with the regularity of the special treatment. Muscle charting and estimation of progress of recovery of paralysis is noted at intervals varying from three to six months according to the duration of the disease, or at any time earlier if requested by the physiotherapist in charge, to attend to some special point arising during the treatment.

A. Relief of pain and stiffness.

A recent case is first placed in a warm bath and movements started in order to (a) relieve pain and stiffness as much as possible; (b) prevent contractures of the stronger muscles and the development of deformities. When pain persists in spite of the hot baths, relief and more adequate treatment is sometimes obtained by the injection of omnopon before treatment.

B. Circulation and nutrition.

Alternate hot and cold spraying is commenced as soon as the condition allows and exercises are given in warm water, in order to improve the circulation and increase the blood supply to the affected limbs and body as a whole. Large bath and head pillow are needed to keep the patient afloat.

Special care is taken during exercises in bed and in the treatment room and while patients are not receiving treatment to keep them *warm*. In bed the patients should wear warm socks, clothing and have blankets next to them with, if necessary, hot-water bottles.

Results of this treatment.—By increasing the circulation in the limbs, chilblains and trophic skin changes are prevented. Blue limbs do not occur, and wasting appears to be less marked. There is no shortening of the limbs, and by keeping them warm, exercises are made easier.

C. Re-education.

(a) In a warm cubicle, screened from outside influences in order to obtain the child's full co-operation and concentration, exercises are given first in hot water in a large bath, then with the child dried, naked and on flat, hard surface such as a table of suitable height.

(b) Special attention is given to: Good position of whole body during exercises; constant supervision by physiotherapist during sitting, standing or walking exercises, to prevent overstrain and correct any tendency to bad position.

(c) The memory of the movement is maintained by active assisted exercises short of tiring the muscles, and progression is made as power increases.

(d) Great care is taken to assist each and every muscle to perform its own individual movement, and to avoid trick and group movements.

(e) Muscles are found to produce the earliest contraction and increase in strength when worked and exercised in their outer range position but short of overstretching.

(f) Additional exercises are given two to three times daily to the patient in bed.

(g) Resisted exercises are given according to progress of recovery of muscles.

Advantages of exercises combined with hydrotherapy.—(1) Limbs kept warm while exercised; (2) buoyancy allows patient to see results of even smallest contractions and this has a good psychological effect; (3) elimination of gravity; (4) elimination of friction.

D. Prevention of deformities.

Deformities may be caused by the unequal recovery of paralysed muscles and the over-action of normal muscles and there is danger of overstretching by non-co-operating young children, so retentive apparatus must be used when the occasion arises.

The staff are specially trained in: (1) Maintenance of position of patient in bed; (2) prevention of strain when lifting patient to and from bed to trolley and treatment room.

Methods.—(1) Patients are maintained in recumbent position of rest when not receiving exercises by: (a) Lying on bed provided with fracture board and sorbo mattress to give firm surface and prevent sagging; (b) knee pillow to prevent hyperextension of knee; (c) back pillow to prevent lumbar kyphosis; (d) footboard to prevent footdrop; (e) arm pillow to maintain normal alignment; (f) sandbags to prevent rotation and inversion or eversion of foot; special restrainers are used to keep patient flat and to keep feet down to the footboard.

(2) Special frame restrainers for young children: (a) Fix shoulders and pelvis; (b) make fixation for foot and arm possible; (c) make correction of deformity possible;

The next point which impressed me was that spotty or isolated muscle paralysis did not develop in her cases. I was further struck by the remarkably healthy appearance of the individuals who had been under her treatment. Those who had no residual paralysis presented themselves as excellent specimens of humanity. Those with residual paralysis showed less involvement than would have been expected in a similar series of patients treated by other methods.

I believe these procedures are a valuable addition to physiotherapy. The patients who receive this treatment are much more cheerful than those treated with splints, plaster, and other forms of treatment. I want to emphasize that none of the cases had had operative procedures, and in the first group of 84 cases I do not know what operations any orthopædist would have performed. There were no flexion deformities, no scolioses. There were a few flail joints, but the patients all handled themselves very nicely with crutches and did not require braces. This series, of course, is much too small for any final conclusions to be drawn. I hope that I may return there some day and see the end-results of as many of these cases as possible.

Mr. Eric I. Lloyd: The anterior horn cells are picked out in anterior poliomyelitis and a greater or lesser number die finally and completely; we know of no method of resurrecting them. If all the cells supplying a muscle or group of muscles are thus fatally struck down then that muscle or group of muscles loses its function of contracting and becomes completely and permanently paralysed.

Fortunately, the blow is often less lethal, though more widespread than this, and many anterior horn cells are not dead but are temporarily out of action. This is perhaps due to a combination of the physical effects of œdema and the chemical effects of toxæmia. The difference between death and loss of function is the key to the course which the disease runs, and is well illustrated by familiar differences between apparently similar paralyses elsewhere. A fracture of the middle third of the humerus may cause complete radial nerve paralysis which is permanent if the nerve is divided, but temporary and recoverable if the nerve is merely stretched, œdematous or bruised. The same is true of the facial nerve in mastoid disease and the external popliteal and ulnar nerve in the everyday postural or traumatic paresis.

Treatment.—We cannot raise the dead anterior horn cells, and we can do very little, if anything, to speed the recovery of the adjacent cells which are going to recover in any case.

Thus it comes about that paralysis is maximal in the early stages of the disease and that some recovery may be expected in every case. Recovery varies clinically from 99.9 to 0%.

The effects of this disaster to the anterior horn cells will vary with the concentration in an area, and the same number of dead anterior horn cells might in one patient cause a complete foot drop and in another a very slight general muscular weakness of the whole limb.

Recovery is due to the surviving anterior horn cells and the muscle fibres which they supply, taking over the function of those which are dead. The surgeon and masseuse aim to exercise and develop these fibres by every available means which stop just short of fatigue.

There is here, however, the important difference that we must safeguard the paralysed muscles from being overstretched by their opposers and that we must prevent the opposers from shortening abnormally and thus causing the joints to get into bad positions, which may become permanent. The weight of the limb (gravity) is another force which must be either harnessed to pull in the right direction, or hindered from pulling in the wrong one.

Rest, posture, splints, plaster, assisted and resisted exercises, re-education, heat, cold and even electricity may be used.

Operation can be considered when either all spontaneous recovery has ceased, or two years have elapsed since the onset of the disease—whichever is the longer.

The unanimous conclusions of myself and some co-workers with regard to Sister Kenny's methods were published in the *British Medical Journal* (1938 (ii), 852) and subsequent events have, I think, done nothing to modify the opinions therein expressed. The report was based upon the study of 55 examples of the disease and 34 of them were considered recent, inasmuch as treatment started within eight weeks of the onset of the disease.

Dr. Q. I. E. May (Carshalton): The unit of Queen Mary's Hospital was re-organized by Miss Kenny, then further developed but still using some of her methods.

The unit consists of three wards of 18 patients each and a treatment room with a team of workers comprising the medical staff, 7 physiotherapists, sisters, nurses and a porter; all of whom except the medical staff work full time on a treatment which is continuous every day of the week including Sunday.

On admission as early as possible after the onset of the disease a preliminary examination and discussion of the patient is undertaken by this team together to determine: (1) Extent of paralysis and the charting of muscle power; (2) the course of future treatment; (3) the method of maintaining position in bed.

Thereafter a general examination is made at frequent intervals, special care being taken to maintain good health and freedom from intercurrent infection, which seriously interferes with the regularity of the special treatment. Muscle charting and estimation of progress of recovery of paralysis is noted at intervals varying from three to six months according to the duration of the disease, or at any time earlier if requested by the physiotherapist in charge, to attend to some special point arising during the treatment.

A. Relief of pain and stiffness.

A recent case is first placed in a warm bath and movements started in order to (a) relieve pain and stiffness as much as possible; (b) prevent contractures of the stronger muscles and the development of deformities. When pain persists in spite of the hot baths, relief and more adequate treatment is sometimes obtained by the injection of omnopon before treatment.

B. Circulation and nutrition.

Alternate hot and cold spraying is commenced as soon as the condition allows and exercises are given in warm water, in order to improve the circulation and increase the blood supply to the affected limbs and body as a whole. Large bath and head pillow are needed to keep the patient afloat.

Special care is taken during exercises in bed and in the treatment room and while patients are not receiving treatment to keep them *warm*. In bed the patients should wear warm socks, clothing and have blankets next to them with, if necessary, hot-water bottles.

Results of this treatment.—By increasing the circulation in the limbs, chilblains and trophic skin changes are prevented. Blue limbs do not occur, and wasting appears to be less marked. There is no shortening of the limbs, and by keeping them warm, exercises are made easier.

C. Re-education.

(a) In a warm cubicle, screened from outside influences in order to obtain the child's full co-operation and concentration, exercises are given first in hot water in a large bath, then with the child dried, naked and on flat, hard surface such as a table of suitable height.

(b) Special attention is given to: Good position of whole body during exercises; constant supervision by physiotherapist during sitting, standing or walking exercises, to prevent overstrain and correct any tendency to bad position.

(c) The memory of the movement is maintained by active assisted exercises short of tiring the muscles, and progression is made as power increases.

(d) Great care is taken to assist each and every muscle to perform its own individual movement, and to avoid trick and group movements.

(e) Muscles are found to produce the earliest contraction and increase in strength when worked and exercised in their outer range position but short of overstretching.

(f) Additional exercises are given two to three times daily to the patient in bed.

(g) Resisted exercises are given according to progress of recovery of muscles.

Advantages of exercises combined with hydrotherapy.—(1) Limbs kept warm while exercised; (2) buoyancy allows patient to see results of even smallest contractions and this has a good psychological effect; (3) elimination of gravity; (4) elimination of friction.

D. Prevention of deformities.

Deformities may be caused by the unequal recovery of paralysed muscles and the overaction of normal muscles and there is danger of overstretching by non-co-operating young children, so retentive apparatus must be used when the occasion arises.

The staff are specially trained in: (1) Maintenance of position of patient in bed; (2) prevention of strain when lifting patient to and from bed to trolley and treatment room.

Methods.—(1) Patients are maintained in recumbent position of rest when not receiving exercises by: (a) Lying on bed provided with fracture board and sorbo mattress to give firm surface and prevent sagging; (b) knee pillow to prevent hyperextension of knee; (c) back pillow to prevent lumbar kyphosis; (d) footboard to prevent footdrop; (e) arm pillow to maintain normal alignment; (f) sandbags to prevent rotation and inversion or eversion of foot; special restrainers are used to keep patient flat and to keep feet down to the footboard.

(2) Special frame restrainers for young children: (a) Fix shoulders and pelvis; (b) make fixation for foot and arm possible; (c) make correction of deformity possible;

(d) aid nursing, specially avoiding constant lifting for bedpans; (e) keep patient warmer; (f) are easily adjustable.

E. Muscles.

These are not expected to bear weight until they are considered to have reached a reasonable state of recovery by the doctor and physiotherapist, and this time varies for each child. Then intensive exercises may be given to obtain maximum function possible, but all the time bearing in mind that fatigue must be avoided. These exercises may be given in classes if there are sufficient children suitable.

When muscles show no prospect of further recovery and are incapable of carrying out their proper function, appliances are resorted to and operations are performed.

Dr. E. W. Neill Hobhouse: Some years ago I had the honour of representing the Children's Section in a meeting on poliomyelitis, when Dr. Jensen gave his report on the 1934 epidemic in Denmark (*Proceedings*, 1935, **28**, 1007). In the discussion which followed, such attention as was paid to treatment was focused almost entirely on one point, which was the burning question of that time. It is of interest to me to note that this question has not even been mentioned by any of the speakers to-day, and I think it is perhaps good discipline for us to wonder how much of our therapeutic views of to-day will feature in a discussion in 1950. The question to which I refer was the use of convalescent serum, and we should remember that this treatment could claim emphatic support from authoritative sources in many parts of the world, and statistics were produced from time to time which made it difficult to discard it.

Of the other attempts to combat poliomyelitis in the early stage none has established itself on the evidence of observed fact. In the treatment of this stage I am forced to the unsatisfactory conclusion that one's function is limited to preventing further mischief from taking place before the period of convalescence arrives.

On treatment in the early convalescent stage there still appears to be considerable difference of opinion. We all agree that the most important element in it is active movement, but we differ as to when it should start. Our difficulty here is that the exact pathology of that period is obscure. We can get a good idea of the course of the inflammatory process from sections in the monkey, and can correlate this with changes in the cell count in patients. But that curious progressive rise of the protein which succeeds the inflammatory process—characteristic of virus diseases involving the lower motor neurone—must be significant of some reaction of the tissues, but the significance remains obscure. In the absence of any scientific criterion of the termination of active disease I think we are wise to fall back on the cessation of muscular tenderness as the best test available.

The hope placed in convalescent serum was born of the belief that this was a bloodborne disease. I imagine that future experiment may be associated with intestinal antiseptics, the value of which has always been exceptionally difficult to assess. I believe myself that errors in diagnosis have hampered research to a considerable extent. I have seen on many occasions in consultation and in hospital a child with an absent knee-jerk, a weak though not paralysed limb, in whom a diagnosis of poliomyelitis had been made or suggested; muscular wasting was not present and electrical reactions were normal: the child was suffering from a benign virus infection which broke the reflex arc on the afferent side. If one of these cases of encephalomyelitis is treated as poliomyelitis it will inspire confidence in any form of therapy applied, for most of them recover completely without any treatment at all. It is of great importance that no case should be used as evidence of the value of treatment unless involvement of the lower motor neurone is established by electrical change or unmistakable muscular wasting.

Dr. Ursula Blackwell said that cases of poliomyelitis received at the Western Hospital were kept for about a fortnight, unless they had respiratory difficulties. Formerly, treatment was by immobilization, either by splints or plasters, and patients then went to the orthopædic hospital after about two to three months. This was not altogether satisfactory, and when Sister Kenny was invited over by the London County Council, the speaker and others went to Carshalton and after that visit the Kenny method was tried at the Western Hospital. Splints and plasters were rarely used and treatment consisted in fixing a board to the bottom of the bed and giving hot packs for a quarter of an hour every two hours in the day and every four hours at night. Old blankets were used and no case of scalding or over-heating had occurred. An enormous staff was required for this treatment, a thing difficult at present. The spray treatment was now being tried, as described by Dr. May. Great difficulty had been experienced in keeping the foot in position against the board unless by sandbags or by means of a sandal fixed to it, as used by Sister Kenny, which was in a sense a splint. In a fair number of cases diagnosis was not confirmed, a few

being the sequel to diphtheria immunization, though clinically they were sometimes indistinguishable from poliomyelitis.

Dr. E. S. Evans thought there were one or two points about Major Stewart's remarks which called for criticism. One concerned the symmetrical distribution of the paralysis around the joints, and the inference that in Sister Kenny's cases this did not occur. There was no doubt that looking at the cases now treated at Carshalton under the modified system and comparing the procedure with what took place at Carshalton ten or fifteen years ago, when he was there before, great improvements had been effected. One was the absence of scoliosis following the treatment. Major Stewart had made it clear that in his own clinic he was getting scoliosis in certain cases, whereas no such cases occurred under Sister Kenny's method. Major Stewart was carrying out orthodox orthopædic treatment. In this country at the moment one would say that the orthopædic treatment, where trunk muscles were concerned, was the treatment of expediency. He was not sure whether Sister Kenny had gone further than that at all, but at Carshalton at the moment scoliosis did not develop during the course of treatment. The cases had been there, generally speaking, up to two years, and what the end-results would be no one, of course, could tell.

Another point of improvement was in the circulation. Again there was no question as to this compared with the conditions obtaining ten or fifteen years ago. But in the general conception of practice at the present time people were much more prepared to carry out treatment in warm rooms and by means of warm baths, whereas years ago it was very different.

He saw a number of cases at the Queen Elizabeth Training College for the Disabled, Leatherhead, and there one saw the ordinary "blue limb" and trophic changes and chilblains. He thought altogether that the form of treatment now in vogue was better than any other hitherto available and a debt was owing to Sister Kenny for having ventilated that treatment. Her action did stimulate the London County Council to provide a unit for children afflicted with this disease, and she deserved their thanks for guiding them in providing intensive treatment. As a result he thought that, with the improvement of circulation, the muscle fibres which recovered probably hypertrophied and recovered to a greater extent than in the old days.

Dr. G. H. Newns said that he had always believed in moving the limbs as early as possible in poliomyelitis. He was surprised to see, earlier in the war, a series of 12 to 15 cases in a base hospital treated by means of prolonged immobilization in plaster casts for periods varying from four to six months. He had been told that the rationale of this method of treatment was the prevention of overstretching of paralysed muscles. It was considered that the danger of fixation of joints as a result of this prolonged immobilization was minimal in children.

Dr. Newns thought that this was an extreme form of treatment: the danger of overstretching of muscles could be guarded against by the performance of passive movements which should be carried out by expert masseuses. Moreover joint fixation was by no means unknown in children.

The meeting had shown general agreement that movements at an early stage—that is as soon as muscular tenderness had subsided—combined with the application of heat to the limb by means of warm baths, &c., gave the best hope of a good functional result. It seemed that this treatment did not give rise to deformities such as scoliosis or foot drop.

It was his view also that splintage should be minimal and that the limbs should be moved at an early stage in the disease.

Mr. F. C. Durbin spoke as one who himself had suffered from the disease. The fear of prolonged invalidism prompted him to exercise as much as possible every muscle he could. He had physiotherapy for only six weeks, but he exercised the muscles himself and he made a good recovery. He thought that treatment should be on the lines of minimum splintage and movement at the earliest opportunity.

Dr. P. Bauwens, from the Chair, said that Mr. Eric Lloyd had drawn a misleading analogy between the radial nerve injury and anterior poliomyelitis. If one cut the radial nerve one blocked both the afferent and the efferent impulses. With an anterior poliomyelitis the afferent part of the system remained intact so that stimulation of the skin went on causing vasodilatation, and stimulation of the spindles in the paralysed muscle would still produce an inhibitory state around the anterior horn cells which supplied the

antagonists. There was just a possibility that movement, either voluntary or passive, in the paralysed muscle would cause inhibition of the antagonists, resulting in a reduction of spasm. He only put this forward in a tentative manner. It was also possible that the cerebral impulses, which seemed to be of some importance, although they never reached the muscle, did produce an inhibitory state in the anterior horn cells supplying the antagonists. Thus, if one concentrated on the movement of a paralysed muscle, one might prevent the contracture of the antagonists.

Major W. J. Stewart, in replying on the discussion, said that he was not aware of any flexion contractures in the acute cases which were treated consistently by this type of physiotherapy. He thought that some of the members of the Department of Physiotherapy in Minnesota were interested in investigating the muscle itself in acute cases of poliomyelitis.

One speaker had said that scoliosis developed only in ambulatory cases. He himself had seen scoliosis develop in bed, both in his own cases and in other clinics. Having definite ideas about what might occur during rest in bed he thought that these cases should, as far as possible, have no restriction of their movements. Extensive plaster fixation should be abandoned.

As soon as the individual was free from pain, movement was encouraged in all muscles. All the movements began as passive movements, and then, within a few weeks active movements were encouraged. Each joint was put through one complete range of movement twice a day. During the rest of the time the individual moved around the bed, sat up, and did anything he wanted to do. There was no restriction placed on voluntary movements.

In regard to the use of hot packs, it was sometimes very hot in Minnesota, but if pure woollen blankets were used there appeared to be little danger of scalding the patient, and when a patient was sick he tolerated heat very well. When he began to get better he responded much more to the administration of heat, and then the packs caused discomfort. They had some cases of extensive furunculosis in children. This happened in about 10% of the cases. He added that the outside temperatures in Minnesota sometimes went up to 105°, but he had not known any untoward results from heat. Cooling devices such as fans were in use.

As to time of commencement of treatment, many of their cases were received within three or four days of the onset of the disease. Some were apparently very ill patients, and some of them had ascending paralysis up to the point of involvement of the intercostal and respiratory muscles. He actually saw two cases taken out of a respirator, without which they appeared hardly able to breathe. But within twenty-four or forty-eight hours of hot fomentations these patients were able to continue without the respirator. Most of the cases were received during the first week or ten days, some of them earlier than that.

Mr. Eric Crook (President of the Section for the Study of Disease in Children) said that his conclusion after hearing the discussion was that Sister Kenny's treatment did not introduce any fundamentally new principles. The hot pack applied intelligently could not do any harm. They all approved of the principle of heat and of keeping the muscle warm, so long as the heating did not irritate or burn the skin. One had always thought that any local irritation during the acute stage must have some harmful effect on the anterior horn cells, but if that was not carried to excess it might be beneficial. Sister Kenny, he believed, did splint when necessary. With regard to muscle movement, she started earlier on this than was the usual orthodox practice. But in orthodox treatment they had always advocated voluntary movement at as early a stage as they felt to be safe.

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[January 25, 1944]

DISCUSSION ON THE CLINICAL APPROACH TO INDUSTRIAL MEDICINE

Dr. Donald Hunter: In the evolution of our industrial civilization it is surely remarkable that hospitals and universities have done so little to study the effects of occupation upon health. The criticism applies with equal force to research and to teaching. Perhaps Hippocrates was to blame!

There is good evidence that the ancient Greeks despised the working man and that, as a result of this attitude, a decline in the social status of the manual labourer accompanied the growth of civilization. Socrates delivered the following judgment on manual work and the manual worker. "What are called the mechanical arts carry a social stigma and are rightly dishonoured in our cities. For these arts damage the bodies of those who work at them or who have charge of them, by compelling them, indeed, in some cases to spend the whole day by the fire. This physical degeneration results also in deterioration of the soul. Furthermore, the workers at these trades simply have not got the time to perform the offices of friendship or of citizenship. Consequently they are looked upon as bad friends and bad patriots. And in some cities, especially the warlike ones, it is not legal for a citizen to ply a mechanical trade."

Obviously a social division so deep as this could not have been without effect on the science and practice of medicine. Hippocrates considered the problem of health on too narrow a basis for he assumed that the patient had nothing to do but to eat, drink, and amuse himself. He developed a theory that health depends upon a balance of food and exercise. But the foods which he discussed are much too elaborate to suggest the diet of a potter or a peasant, and the exercises which he recommended have nothing to do with work. Two thousand years later Ramazzini was to make good the omission of Hippocrates. He inquired in detail into the wretched conditions of workmen in the town of Modena and decided that many arts were the cause of grave injury to those who practised them. As the result of this work he made a striking addition to the Hippocratic art: "When a doctor visits a working-class home he should be content to sit on a three-legged stool, if there isn't a gilded chair, and should take time for his examination; and to the questions recommended by Hippocrates he should add one more—'What is your occupation?'"

With the rise of industrialism in the nineteenth century, the worker was protected against long hours of work, inadequate ventilation, and accidents, by the passing of the Factory Act in 1844. Since then, the conditions in British industry have compared very favourably with those in any other country. From 1878 onwards provisions were made to control dangerous trades by so-called special rules of the Home Office. The early knowledge of industrial diseases was obtained by placing an obligation on the medical practitioner and employer to notify them to the Chief Inspector of Factories. Between 1896 and 1927 eleven diseases were made notifiable. It was during this time that Sir Thomas Legge did his outstanding work as the first Medical Inspector of Factories. There are now some 43 scheduled diseases under the Workmen's Compensation Acts which are wider in scope than the Factories Act. The Factory Department of the Ministry of Labour which has played a vital rôle in British health legislation is doing excellent work under difficult conditions. It has 387 lay and 13 medical inspectors to deal with some 250,000 establishments covered by the Factories Act of 1937. It numbers on its staff men and women who are among the greatest living authorities on different aspects of industrial hygiene and toxicology.

The twentieth-century physician must know something of the dangers which may occur in the chemical, aircraft, munitions, plastics and textile industries. The present rate of industrial development demands the frequent discovery of new materials. The substances produced rapidly become indispensable, but their properties may remain for a long time insufficiently understood. Some of them are dangerous under certain conditions: how dangerous has on several occasions not been realized until a fatal accident has occurred. It therefore happens that the doctor practising in an industrial area may have to deal with patients exposed to substances which until recent years were little more than chemical curiosities, including aromatic nitro- and amino-compounds, chlorinated hydrocarbons, ketones, and glycol derivatives, some of which are harmless and others so deadly that their use might with advantage be forbidden. Some are absorbed by inhalation, others through the skin: some attack the liver, causing toxic jaundice, others the kidneys causing suppression of urine: some affect the blood, causing methæmoglobinæmia with lilac cyanosis; others attack the bone-marrow, causing thrombocytopenia, leucopenia, and aplastic anæmia. But such diseases are not common. No case

of poisoning by coal tar benzene has ever been admitted to the London Hospital, and the records go back to 1860. We are investigating the benzene hazard in the dope shops of aircraft factories of various types. The concentration of benzene in the atmosphere is too small to cause harm, and blood-counts show that there is no more anæmia in the girls who use the spray guns than in control subjects. In both groups it is a mild low colour-index anæmia, and in both recovery is rapid when the patient is treated with iron.

Whether he works in a factory or not the clinician must know something of the chemistry of industrial processes, and of the toxicological risks in dangerous trades. For example the metallic poisons have entirely different effects depending on whether they exist in organic or inorganic form, whether their physical properties are those of a solid, a liquid or a gas, whether the valency of the metal radicle is high or low, and whether they fall upon the skin or enter the body through the respiratory or alimentary tracts. Industrial arsenic poisoning occurs in two forms, the first from inhalation of or contact with the dusts of compounds of arsenic, and the second from inhalation of arseniuretted hydrogen. The symptoms in the two groups bear little or no resemblance to one another. The compounds of arsenic act as local irritants to the skin and mucous membranes, giving rise to dermatitis, papilloma and even carcinoma of the skin, conjunctivitis, coryza, laryngitis and even perforation of the nasal septum. Polyneuritis does not arise, and only rarely is the dose of arsenic large enough to produce the gastro-enteritis so common in the criminal administration of arsenic. Arseniuretted hydrogen, on the other hand, acts as a powerful hæmolytic agent, causing hæmoglobinuria, anæmia and hæmolytic jaundice. The well-known symptoms of poisoning by inorganic compounds of lead are entirely absent in men poisoned by tetra-ethyl lead. This is an organic, lipoid-soluble compound and is absorbed directly through the skin. It gives rise to restlessness, talkativeness, ataxia, insomnia, delusions and mania, but not to wrist-drop, colic or anæmia.

Men poisoned by organic derivatives of mercury do not show the clinical symptoms of poisoning by the metal itself, namely, salivation, stomatitis, and erethism. In 1937, four men were admitted to my ward showing symptoms and signs of a unique disease of the nervous system; there were severe generalized ataxia, dysarthria and gross constriction of the visual fields; memory and intelligence were unaffected. They had been employed in the manufacture of methyl mercury iodide for use in agriculture as a fungicidal dust in the prevention of certain smut diseases of cereals. The precautions used in the factory against inhalation of dusts and vapours were inadequate. The selective effect of the poison on certain parts of the nervous system was confirmed by experiments in which rats and a monkey were exposed to the vapour of methyl mercury iodide. This caused an intense and widespread degeneration of some of the sensory paths of the nervous system, the peripheral nerves and posterior spinal roots being affected first and the dorsal columns of the spinal cord and some of the neurones in the middle lobe of the cerebellum later. In the manufacture of organic mercury compounds adequate precautions must be taken to ensure that dust and vapours do not come in contact with the skin and are not inhaled. The use of gloves and respirators is inadequate as a means of protection; the whole process of manufacture, including the final packing of the dust, should be carried out mechanically in enclosed apparatus.

The industrial doctor of the future must have close links with the main chain of general medicine. Academic centres of industrial medicine will arise as in the new organization set up by the Medical Research Council in the London Hospital. In several of the larger industrial areas of Great Britain a physician on the staff of a teaching hospital should be equipped to study and to teach the medical problems of industry. His staff must include whole-time assistants in medicine, chemists, pathologists, statisticians, almoners, and technicians. His equipment must include research grants, pathological and chemical laboratories, an animal house, a museum and a library. He would investigate all suspected cases of industrial poisoning either admitted direct to his wards or referred to him by common consent. His contact with industrial medical officers in his district as well as with the Factory Department of the Ministry of Labour would ensure for him adequate clinical material. He would conduct researches in his wards and laboratories on the toxicity of the numerous chemical substances introduced into industry. Whenever a new chemical substance is on general principles suspect, it must be tested first on experimental animals and not on the workman.

In his work the physician studying industrial medicine would reap the advantages of immediate contact with experimental pathologists, morbid anatomists, pharmacologists, chemists, physiologists, physicists and engineers in the corresponding university departments, as well as with his medical and surgical colleagues. He and his staff would instruct undergraduates in factory welfare, working conditions, toxic hazards, the treatment of accidents, rehabilitation and general sick absence problems. Not only would

he take medical students to factories but also he would arrange a warm welcome for industrial medical officers wishing to attend post-graduate classes in his department and the ward rounds of physicians and surgeons who were his colleagues. He would establish a close liaison with local factories and his department would work in conjunction with that of his surgical colleagues interested in accidents and rehabilitation of the injured workman. By such means should the general practitioner of the future receive adequate instruction in conditions and hazards of factory life. He must realize that he cannot do his best for his patients unless he studies the conditions under which they work in factory, mine, quarry, dock, shipyard, office, shop or the various transport services. Only a fraction of the nation's work is done by large firms and the smaller firms must always look for help to the general practitioner: there is nothing in the nature of industrial medicine which is beyond the competence of a sound practitioner.

The present-day industrialist knows that doctors in general are ignorant of conditions in industry. Too often he regards with contempt and annoyance the efforts of the medical profession to certify illness in his employees. The factory doctor is usually relegated to his ambulance room: the management does not think of him as a trained professional man to be employed in a preventive capacity. No doubt this explains why industrial firms so often aim at conditions which are just tolerable instead of setting out to design a factory with the idea that it should be a joy to work in. The full-time industrial doctor of the future must be so well trained that he will be invited to co-operate with managers, workers, engineers, chemists and architects. He should aim at discovering all possible faults in the working environment with a view to finding proper remedies for them. One of his most interesting duties must be to bring into the effective service of industry the discoveries of the research worker. Only then will he be in a position to make the industrialist understand the risks to which his men are exposed, and that the guiding principle of low costs and large profits retards progress. He should have an aptitude for administration though in the factory he is best employed in an advisory, not an executive, capacity. He should be responsible to the managing director, and not to any other official of the company, such as the labour manager. He should take charge of all first-aid, medical and nursing services. He should have had considerable experience in clinical work and should have held resident hospital appointments: he should know something of social problems and should be able to undertake original research in medicine. His work demands the mind of a physician rather than that of a surgeon or a public health official, and he should therefore hold one of the higher qualifications in medicine such as M.D., or M.R.C.P.

The factory medical officer should never allow his special technical knowledge to assume greater importance than his knowledge of doctoring in general. He should strive to be a good doctor in the broadest sense of the term, to preserve contacts with academic medicine, to cultivate interests outside his profession, and to follow his various activities with a constant regard for social values. As social-mindedness develops a better industrial medical service will be demanded. At present the supply of competent doctors is inadequate to fill the vast number of posts which already exist in factories. Meanwhile the majority of our medical schools and teaching hospitals are not alive to this need.

Dr. Donald Stewart: I wish to approach the subject from the angle of the practising industrial medical officer. Clinical medicine is an essential basis of my work, but closely related the whole time to the social and environmental background of industry. Although there may not be the satisfaction of continued treatment and recovery—found in hospital and general practice—there is much compensation in the preventive and sociological aspects of the work. When Dr. E. R. A. Merewether, in the recent annual report of H.M. Chief Inspector of Factories, said that the industrial medical officer should be as much as possible about the works and as little as possible in his factory ambulance room or surgery, he forgot the considerable clinical problems daily confronting the doctor in industry. This side of the work could best be known by those actually employed in factories. A knowledge of processes is obviously essential, but even after extensive hygiene surveys clinical examination is necessary before advice can be given to the management in connexion with specific toxic hazards, or other factors such as lighting and ventilation. For example, in assessing the potential hazard in iron and steel foundries there has to be extensive clinical and X-ray examinations. Industrial medicine therefore, in recruiting new entrants, should aim at obtaining men of the widest clinical experience.

Including the armed forces there are 22½ million persons in the country employed in whole-time national service. If there are 10 million workers in industry (and there are probably more), 7½ millions are occupied in factories; the remainder work in mines, quarries, railways, shipping, docks and construction, as commercial and clerical workers, and in agriculture. Industrial medicine must cover all these trades and occupations, and all sizes of groups of workers.

of poisoning by coal tar benzene has ever been admitted to the London Hospital, and the records go back to 1860. We are investigating the benzene hazard in the dope shops of aircraft factories of various types. The concentration of benzene in the atmosphere is too small to cause harm, and blood-counts show that there is no more anæmia in the girls who use the spray guns than in control subjects. In both groups it is a mild low colour-index anæmia, and in both recovery is rapid when the patient is treated with iron.

Whether he works in a factory or not the clinician must know something of the chemistry of industrial processes, and of the toxicological risks in dangerous trades. For example the metallic poisons have entirely different effects depending on whether they exist in organic or inorganic form, whether their physical properties are those of a solid, a liquid or a gas, whether the valency of the metal radicle is high or low, and whether they fall upon the skin or enter the body through the respiratory or alimentary tracts. Industrial arsenic poisoning occurs in two forms, the first from inhalation of or contact with the dusts of compounds of arsenic, and the second from inhalation of arseniuretted hydrogen. The symptoms in the two groups bear little or no resemblance to one another. The compounds of arsenic act as local irritants to the skin and mucous membranes, giving rise to dermatitis, papilloma and even carcinoma of the skin, conjunctivitis, coryza, laryngitis and even perforation of the nasal septum. Polyneuritis does not arise, and only rarely is the dose of arsenic large enough to produce the gastro-enteritis so common in the criminal administration of arsenic. Arseniuretted hydrogen, on the other hand, acts as a powerful hæmolytic agent, causing hæmoglobinuria, anæmia and hæmolytic jaundice. The well-known symptoms of poisoning by inorganic compounds of lead are entirely absent in men poisoned by tetra-ethyl lead. This is an organic, lipoid-soluble compound and is absorbed directly through the skin. It gives rise to restlessness, talkativeness, ataxia, insomnia, delusions and mania, but not to wrist-drop, colic or anæmia.

Men poisoned by organic derivatives of mercury do not show the clinical symptoms of poisoning by the metal itself, namely, salivation, stomatitis, and erethism. In 1937, four men were admitted to my ward showing symptoms and signs of a unique disease of the nervous system; there were severe generalized ataxia, dysarthria and gross constriction of the visual fields; memory and intelligence were unaffected. They had been employed in the manufacture of methyl mercury iodide for use in agriculture as a fungicidal dust in the prevention of certain smut diseases of cereals. The precautions used in the factory against inhalation of dusts and vapours were inadequate. The selective effect of the poison on certain parts of the nervous system was confirmed by experiments in which rats and a monkey were exposed to the vapour of methyl mercury iodide. This caused an intense and widespread degeneration of some of the sensory paths of the nervous system, the peripheral nerves and posterior spinal roots being affected first and the dorsal columns of the spinal cord and some of the neurones in the middle lobe of the cerebellum later. In the manufacture of organic mercury compounds adequate precautions must be taken to ensure that dust and vapours do not come in contact with the skin and are not inhaled. The use of gloves and respirators is inadequate as a means of protection; the whole process of manufacture, including the final packing of the dust, should be carried out mechanically in enclosed apparatus.

The industrial doctor of the future must have close links with the main chain of general medicine. Academic centres of industrial medicine will arise as in the new organization set up by the Medical Research Council in the London Hospital. In several of the larger industrial areas of Great Britain a physician on the staff of a teaching hospital should be equipped to study and to teach the medical problems of industry. His staff must include whole-time assistants in medicine, chemists, pathologists, statisticians, almoners, and technicians. His equipment must include research grants, pathological and chemical laboratories, an animal house, a museum and a library. He would investigate all suspected cases of industrial poisoning either admitted direct to his wards or referred to him by common consent. His contact with industrial medical officers in his district as well as with the Factory Department of the Ministry of Labour would ensure for him adequate clinical material. He would conduct researches in his wards and laboratories on the toxicity of the numerous chemical substances introduced into industry. Whenever a new chemical substance is on general principles suspect, it must be tested first on experimental animals and not on the workman.

In his work the physician studying industrial medicine would reap the advantages of immediate contact with experimental pathologists, morbid anatomists, pharmacologists, chemists, physiologists, physicists and engineers in the corresponding university departments, as well as with his medical and surgical colleagues. He and his staff would instruct undergraduates in factory welfare, working conditions, toxic hazards, the treatment of accidents, rehabilitation and general sick absence problems. Not only would

disease, and as a guide to treatment, which should be planned with special reference to the physical requirements of the patient's work.

The psychological factor in disability.—Malingering is so rare as to be almost left out of account, but many injured people display a reluctance to use the injured part which cannot be ascribed to any local defect, and betokens an abnormal state of mind. This often arises from mere ignorance—the patient does not know, because he has never been told, what is wrong with him, what was found by X-rays, what was done at operation, or what he can do to help himself to recover. He is bewildered and frightened by the strange experience of being hurt, and by the still more strange procedures to which he is thereafter subjected by the doctor, and so may easily develop a neurosis, the pattern of which is determined by his temperament—it may be morbid self-pity, an aggressive attitude, or a conversion hysteria. Unfortunately, some neurologists seem to take little interest in a patient who shows no signs of organic disease, while the treatment of neurosis by patient explanation and re-education takes a great deal of time, and hence many cases are left to make their own slow and inadequate adjustment, not only unaided, but even deterred by inappropriate treatment such as prolonged massage for a few hours per week. The important thing to realize is that post-traumatic neurosis is almost always preventible, and so ought to be prevented. It is difficult to cure, full recovery may be expected only in some 20-30% of cases, about 50% improve, and in the remainder the nervous symptoms persist indefinitely; some get worse, even after settlement of the claim, especially if this is long deferred.

Structure and function.—Nothing but long experience and careful observation of men at work will enable the industrial medical officer to assess the effect of various physical handicaps on earning capacity. Thus, a tender scar on the tip of the left little finger may completely incapacitate a pianist, but the loss of the whole right upper limb may interfere not at all with the work of a liftman or messenger; it is less obvious that only in a few jobs, such as that of plasterer, it is necessory to have full abduction at the shoulder—an ankylosed shoulder does not prevent a man swinging a sledge-hammer. Amputation through both forearms offers a formidable problem in rehabilitation, but several such cases have been successfully trained and placed in full employment as engineers' draughtsman and even as shorthand-typist and book-keeper; in 1942 persons so trained and placed by the Queen Elizabeth's Training College for the Disabled included 31 with amputations of the lower limb and 23 with upper limb amputations (including 18 above the elbow); most of the latter group undertook welding or spray-painting. It is necessary to make careful inquiries into the patient's preferences and previous experience in selecting a suitable course of training, and close touch must be maintained with employers, who are encouraged to visit the Training College and explain the special requirements of the work. Members of the College Staff and ex-trainees attend employers' conferences and demonstrate the capabilities of the disabled to carry out skilled work.

Medical men are too much inclined to estimate disability in terms of anatomical defect, and to assume that deformity or restriction of movement must necessarily imply some reduction in working capacity; this is far from being the case; the important thing to ascertain is not so much what structure or function has been lost but what remains, and to ensure that this is fully used. Far too often a patient with one injured limb is allowed to forget that he has three uninjured limbs, which ought to be vigorously exercised while the injured one is being treated. We are still far too often guilty of treating the injury, instead of the patient, with the result that the injury recovers while the patient deteriorates.

What can and should be done by the State.—The Tomlinson Report (on the Rehabilitation and Resettlement of Disabled Persons) called attention to "The need for more information than is at present available as to the suitability of particular disablements to particular occupations" and went on to recommend that "A comprehensive survey is essential to a satisfactory resettlement scheme", and to suggest that the Ministry of Labour and National Service should examine this question and consider what would be the best way of collecting this information and "Making it available to the Employment Exchanges". In pursuance of this and cognate objects the Disabled Persons (Employment) Act, 1944, provides for the setting up of a National Advisory Council "With the duty of advising and assisting the Minister in matters relating to the employment, undertaking of work on their own account, or training, of disabled persons".

Procedure under the Workmen's Compensation Acts lends itself all too readily to the idea of a workman who has "partially recovered" from an injury as being fit for an inferior kind of job, at a lower wage, and thus affording an excuse to the employer to reduce the amount of compensation paid. Many medical men feel that it is embarrassing and undignified to be called upon to assist in the administration of these Acts, especially if this entails giving evidence in a County Court. There is a strong

Industrial medicine exists for the immediate treatment of accidents, their follow-up and rehabilitation of the injured; and for the prevention of ill-health and absenteeism. There are half a million accident cases a year on compensation. But the incidence of minor injuries is much greater; for example, in a group of 100,000 workers in Birmingham half a million injuries occurred annually which did not need treatment in hospital. H. M. Vernon has estimated that the number of compensation cases multiplied by 40 gives some index of true accident frequency.

In the prevention of ill-health pre-employment medical examination is important, not to exclude a man from work, but to fit him into a proper job if possible. Placement of workers is coming on to a more scientific basis, and the medical profession must play a part in this. Examination of juveniles under the statutory scheme is not sufficient; there must be an adequately planned follow-up system if preventive medicine is to play its fullest part; with such re-examination schemes there is a drop in labour turnover (which provides a good economic basis for their institution), and higher standards of health result, because illness and accident can be greatly prevented. Here is a vital link with social medicine. The industrial nurse plays an important part in the examination of women. The Essential Work Order has meant much extra work for the factory doctor, which will be continued if there is post-war restriction of labour movement. Group examinations, for example mass examinations by X-ray, will play a greater part than hitherto, and will be an important medium for research development. The study of working environment is a fundamental part of industrial medicine. The Factories Act is in many ways a textbook of preventive medicine. Properly planned health surveys in factories are of great value to employer, worker, and medical and welfare services; these cover factual statements regarding cleanliness, overcrowding, ventilation, heating, lighting, sanitation, dusts, fumes, liquids, noise, weight-lifting, posture problems, seating, boredom, hours of work, and canteens. These factors all affect the individual, but in different ways. The effects can only be determined by an adequate clinical approach, case by case, and group by group. To be in any way convincing, evidence of ill-health must be based on statistically significant data.

There is a great field for industrial health research. To take iron and steel foundries as an example, we know little about the true incidence of silicosis in this basic occupation. Dr. Donald Hunter's department is now tackling this problem, and his efforts will be of the greatest assistance to this section of industry throughout the country. His approach is essentially clinical; but allied with him will be physicists, engineers and production experts. In the final survey, however, clinical medicine will be the paramount factor. The Industrial Health Research Board has recently come to life again after a morbid period. In a bold programme, due in part to the energy of its secretary, it is covering many parts of the field, not the least important of which is the determination of an adequate method of recording absenteeism.

The industrial medical officer, and industry as a whole, need help from the best physicians and surgeons in the country, as well as from factory inspectors and research workers. *Physicians and surgeons themselves must learn more about physical and mental requirements of different occupations*, particularly with regard to rehabilitation and the economics of work. There never was greater need of obtaining an accurate occupational history. Industrial medicine has developed rapidly since the war, but by the demands of workpeople its future place in industry and in medicine is assured. Employers are sometimes slow to appreciate their link with medicine, and further legislation is probably necessary to provide a comprehensive service. Industrial medicine is definitely a personal service. There is great need for well-equipped centres of information *for doctors, industrialists, and workers* in connexion with health problems. Universities have a challenge in this respect, and in the teaching of social and industrial medicine. The problem is to marry the study of the material side (hygiene) with the human side (clinical). The ratio is different in different industries, but the clinical side must eventually be of fundamental importance. Industry wants the best brains of the profession; but to be effective the industrial doctor must keep in touch with clinical medicine. The clinical approach to everyday problems will largely determine the success or failure of this new branch of medicine.

Dr. Donald Norris : Industrial Medicine is concerned with the preservation of the health of the industrial worker, and with the prompt and efficient treatment of any injury or disease which may affect him in connexion with his work. Like every specialist, the industrial medical officer tends to become absorbed in the technical details of his special problems, and he is thus liable to lose touch with the wider and more fundamental principles of medical and surgical science. On the other hand, the physician or surgeon whose work does not bring him closely into touch with industrial conditions may fail to appreciate the importance of these, both as an ætiological factor in

Section of the History of Medicine

President—Sir WALTER LANGDON-BROWN, M.D.

[*November 3, 1943*]

Lavoisier and the History of Respiration

By E. ASHWORTH UNDERWOOD, M.A., B.Sc., M.D., D.P.H.

FEW great scientists have suffered more than Lavoisier from a lack of critical writings on their works. The biography by Grimaux [1] was not published until nearly a hundred years after his death. The complete edition of his *Œuvres* appeared in the years 1864-93 [2]. Berthelot's valuable extracts from Lavoisier's note-books were published in 1890 [3]. Important papers on his work in scientific journals are relatively few. Recently a number of biographies and other studies have appeared—each indebted to Grimaux, and each coloured by the writer's own interests so far as the scientific aspect is concerned; the most valuable are the works of Meldrum, Cochrane, Aykroyd, McKie, French and Hartog [4 to 9]. Nevertheless few of these works deal even briefly with Lavoisier's physiological studies. The celebration of the second centenary of his birth suggests that this aspect should receive more attention, and the following study is pre-liminary to a more extensive work which the writer has in preparation.

The Development of a Brilliant Amateur

Antoine-Laurent Lavoisier was born of good stock in Paris on August 26, 1743. He profited by an excellent education at the Collège Mazarin—one of the few schools which had a good science course. At the University he studied law; but in addition he took voluntary classes in many scientific subjects. Guettard the geologist and Rouelle the chemist especially influenced his further work. To Guettard we owe his final desertion of the law for science; he accompanied Guettard as assistant on a protracted geological tour of France. At the early age of 25 years Lavoisier was elected to the French Academy. Just when he seemed set for a scientific career he took the surprising step of accepting a responsible administrative post in the *Ferme générale*, the wealthy company to which was entrusted the task of farming the nation's revenue. Lavoisier was a capable adminis-trator and business man, and he remained a member of the *Ferme* for twenty-three years, rising steadily to the post of Farmer General. Throughout his life he put in each day sufficient time to get through his administrative work, which often involved much travel-ling; in addition he devoted six hours daily to scientific pursuits.

In 1771 Lavoisier married Marie Anne Pierrette Paulze, a girl of 14 who developed into a brilliant woman. She devoted herself to her husband and his work. She studied Latin and English. She took painting lessons from David, and the figures in the *Traité* were

feeling among those who have had much experience in this field that the time is ripe for a radical revision of the present arrangements for dealing with the legal and economic consequences of industrial accidents, that emphasis should be laid on securing proper treatment rather than on paying "Compensation", and that everything should be done to turn the attention of the injured workman to the prospect of an early return to suitable work, rather than to the glittering prize of a "lump sum". A man with a physical handicap may not have the same wide choice of possible occupation as a wholly able-bodied person, but he usually possesses a residual working capacity, in an appropriate job, which is no less and may even be greater, than that which he had before this defect arose, and which at least is equal to that of his fellow-workers in the same grade. The State can do much, by wise legislation, to provide proper opportunities for the better planning of industrial medical and allied services. All such plans, however, must depend for their efficient execution on the harmonious co-operation of medical men— who must have the necessary special knowledge—with industrialists, and local administrators.

[*November 23, 1943*]

DISCUSSION ON THE STATE OF NUTRITION IN ENEMY-OCCUPIED EUROPE [*Addendum*]

DURING this Discussion (see *Proceedings*, **37**, No. 3, January 1944, p. 117) Dr. Cawadias quoted the rations of various European countries, basing his remarks on the book entitled "Starvation over Europe" published by the Institute of Jewish Affairs in America. In this publication Belgians are quoted as obtaining 67% of their normally required calories.

In reality this figure is erroneous. Belgians got only 47% of the normally required calories during 1943, as shown by the following figures:

Theoretical requirements, calories per head per day 2,600
Actual average intake in February 1943 in calories per head per day 1,240
(i.e. 47% of 2,600)

For reference:
Average diet in Belgium in 1939, calories per head per day 2,868
One should remember also that not everybody can get the official ration.

VALUE OF THE BASIC BELGIAN DIET IN THE FIRST HALF OF 1943

(1) Actual average intake in February and May 1943, calories per head per day ... 1,240
(2) The official basic ration per head and per day in Belgium during February and May 1943. Expansion of figure in (1):

DAILY RATION PER HEAD (BASIC RATION, ADULTS) IN GRAMS

	February	May			February	May
Bread	225	225	Sugar	33·33	33·33
Cereals	9·33	0	Artificial honey*	7·5	15
Butter	6·66	11·66	Jam*	15	20
Margarine	3·33	0	Meat†	30	30
Cheese	5	5	Potatoes‡ ...	500	500

* One only, not both. † Including 20% bone. ‡ The ration of potatoes was supplied since the 1942 harvest but not before.

DAILY RATION IN FEBRUARY 1943 (BASIC RATION, ADULTS) IN CALORIES (*a*)

Bread	445	Cheese	1·93	Meat ...	31
Cereals	31·9	Sugar	112	Dried pulses ...	53·3
Butter	53·9	Artificial honey ...	22	Potatoes	436·0
Margarine	21·42	Jam	32		

Total 1,240·45 calories

These calorie values are given in a report coming from Belgium, but if we use the values given in tables drawn up by the Medical Research Council, we get slightly different results, actually worse, as follows:

Bread	445	Cheese	20·3	Meat ...	99·1
Cereals	31·6	Sugar	126·6	Dried pulses ...	53·3
Butter	49·6	Artificial honey ...	20·7	Potatoes ...	275·0
Margarine... ...	25·6	Jam	37·3		

Total 1,184·1 calories

As artificial honey and jam may not both be purchased only one of their calorie values may be counted. The total for Table (*a*) thus becomes 1,208·45 calories if jam is chosen, or 1,218·45 calories if honey is chosen. Moreover, in those months when no dried pulses are distributed, the total is only 1,155·15 calories or 1,165·15 calories, on the average, 1,160 calories.

If we take the estimate of 1,240 calories (the most favourable one) and compare it with the theoretical needs, 2,600 calories, we find that only 47% of the needs are covered.
—R. LINZ, M.D., D.P.H., *Belgian Ministry of Supply*.

space must be given. His chemical researches must, however, first be dealt with in some detail, since they determined the lines of his physiological work, which would have been impossible had he not paved the way by his brilliant chemical synthesis. It would be easy to discuss in detail the *Mémoires* and the contents of his laboratory journals, but this would require almost a book. The writer has therefore attempted to summarize the main lines of Lavoisier's ideas on chemistry, and it will be seen that in this chemical section his debt to the careful work of Meldrum, of McKie and of Hartog is manifest.

Chemistry was essentially mediæval when Lavoisier was a student. Boyle's definition of an element had remained an abstract conception, and there was no list of elementary substances. Practically the four "elements" of the Greeks and the three "principles" of Paracelsus held the field. It is important to realize that both in chemistry and in physiology the phlogiston theory was a bar to further advances. The theory was first advanced by Johann Joachim Becher in *Physicæ subterraneæ* (1669), and was greatly developed by Georg Ernst Stahl in his *Fundamenta Chymiæ* (1723). On this theory combustion implies the escape of phlogiston from the burning body. Sometimes the process can be reversed. For example, when a metallic calx is heated with charcoal, phlogiston passes from the charcoal to the calx and the metal is reproduced. A metal should therefore be heavier than its calx. Since the time of Boyle it had been known that the reverse was the case, and two alternative explanations of the conflicting facts were in common use. Despite what Lavoisier says [10], there was not really much support for the view that phlogiston had negative weight. Most accepted Boyle's view that increase of weight on calcination was due to the passage of particles of fire through the glass of the retort [11]. The phlogiston theory certainly "explained" many known facts and was an attempt at systematization. As Patterson [12] says, if placed in the position of the philosophers of the time—most of whom except Boerhaave [13] adopted it—we could hardly do otherwise. Another belief of the time was that matter was transmutable. In Van Helmont's willow tree experiment it was shown that vegetable substance was produced from water alone. Boyle's "elastic fluid" was mainly common air; but Van Helmont and Hales had done more than merely suspect that there were different kinds of common air. Yet there was a gleam of true understanding in this darkness. In 1756 Joseph Black published the extended English version of his epoch-making dissertation on *magnesia alba* in which the existence and properties of "fixed air" as a separate entity were clearly demonstrated [14]. His experiments added to the quantitative foundation of the science which had been laid down by Van Helmont and Boyle. The science of chemistry was still saddled with the outmoded names and symbols of the Middle Ages. As Lavoisier later pointed out in the *Méthode de Nomenclature* (1787) it needed much practice and a great memory to remember the substances expressed by some of the current names. Not only were the names *oil of vitriol, butters of arsenic and antimony*, and *flowers of zinc* ridiculous—since there were neither butter, oil, nor flowers in the mineral kingdom; what was worse was the fact that all of these substances are violent poisons [15].

Lavoisier's first chemical paper, published at the age of 21, was an attempt to explain the binding of plaster by analysis of gypsum [16]. It is notable for the fact that he declined to make conjectures which he could not prove. Four years later he began an experiment which was to shake to its foundations the current theory of the transmutability of matter. It had been noted by many chemists that when distilled water was heated in a glass vessel, there was always a slight residue of earthy matter: clearly a case of transmutation of water into earth. By a painstaking experiment Lavoisier showed that the earth came from the glass, and he also obtained some valuable standards of purity for water used in chemical operations [17]. This paper was not actually published until 1773, although that volume of the *Mémoires* was really for the year 1770. A great difficulty in assessing Lavoisier's debt to others, and theirs to him, is this late publication of the *Mémoires*. Hence between the date of the reading of a paper and its actual date of publication it was possible for a member of the Academy to incorporate the results of many later experiments. Lavoisier always took full advantage of this facility—as is seen in his next important Memoir on the combustion of the diamond. He showed that a diamond can be burned, and that the product of combustion is fixed air. This work, though read in 1772, did not appear till 1776 [18].

During this memorable year 1772 other things were happening. In his note-book Lavoisier noted on September 10, 1772, that he had carried out an experiment on the combustion of phosphorus. This was his first attempt at the problem of combustion. On October 20 he presented a note to the Academy informing them of what he was doing, and on November 1, 1772, he deposited a sealed note with the Secretary [19]. Until 1932, when the first two of these notes were published by Meldrum [20], only the last was

drawn and signed by her. David's famous picture (fig. 1) was painted when Lavoisier was 45 and she was 30. As McKie says, in every way she carried enough guns for her husband. The marriage was very happy. In March 1775 Lavoisier was appointed an inspector of gunpowder for the government, and till 1792 he and his wife resided at the house in the Arsenal which they soon made very famous. It was in his own laboratory here that nearly all his scientific work was done and his guidance enabled France to maintain the large stocks of powder which were necessary for the revolutionary wars. He had other interests, including politics. He did much for the Academy, reporting on a considerable proportion of the diverse problems which were submitted to it for investigation. The Lavoisiers were originally of peasant stock, and Antoine always had a deep respect for the habits of the country people. He had a successful experimental farm on his estate

FIG. 1.—LAVOISIER and Mme. LAVOISIER by DAVID. This portrait was painted in 1788, and is now in the Rockefeller Institute, New York. According to Grimaux, it is the only authentic portrait of Lavoisier. [Reproduced by kind permission of the Rockefeller Institute for Medical Research, New York.]

at Fréchines, and in 1785 he became a member of the Committee of Agriculture in Paris. Two years later he was a member of the Assembly of Orleans. Prison and education reform also claimed his attention. Such was the busy life which Lavoisier further enriched by his scientific work, some of which will now be discussed. Throughout his life he remained an amateur in science. At the University he officially studied law, and his scientific studies were voluntary. He never held a paid post in chemistry—except for that at the *Régie des Poudres*, which was largely administrative.

Lavoisier's Chemical Work—The RÉVOLUTION CHIMIQUE

Lavoisier is known to the most junior student as the great founder of the modern science of chemistry. The purpose of this *tribute to his memory is mainly to discuss* some of his other discoveries which are less widely known, and to which therefore most

medically and to raise artificially the temperature of combustion. The actual date of the discovery of "dephlogisticated air" (oxygen) was therefore March 1, 1775 (*see* Hartog [9, 46, 46*a*]). It is important to note that Priestley's first public announcement of his discovery was not made until March 23, 1775, when a letter of his was read to the Royal Society. Fortified by the possession of the key which Priestley had given him the previous August, Lavoisier had meanwhile been repeating Priestley's experiments from the aspect of the hypothesis which he had set out to investigate. On April 26, 1775, he read to the Academy his "Memoir on the nature of the principle which combines with metals during calcination, and which increases their weight" [28]. McKie points out—a statement with which I agree—that Lavoisier here referred to "the purest part of the air", meaning purified air, and not a particular constituent [29]. This paper was revised and read again to the Academy on August 8, 1778, and in the revised form it then appeared in the *Mémoires de l'Académie* for 1775, which was not published until 1778 [30]. In the new version the "purest part of the air" has become "eminently respirable air" and "most salubrious air". He now realized that common air consisted of "eminently respirable air" and an inert *mofette*. In other words, in 1775 Lavoisier had distinguished between oxygen and fixed air, but not definitely between oxygen and common air. Reference will be made later to the experiments which he carried out on the respirability of the new gas. His theory of combustion and calcination dates from 1777.

Fundamental as are the other discoveries of Lavoisier in the history of chemistry, they are not so important with reference to the subject of this paper, and they must therefore be dealt with briefly. In a paper on the combustion of phosphorus published in 1780—but referring to experiments read in 1777—Lavoisier showed that common air could be re-created from the gaseous residue left after combustion—but by the addition of "eminently respirable air" and not "fixed air" as he had previously thought [31]. In 1777 he also began unobtrusively his attack on the phlogiston theory. A memoir which was read on November 23, 1779—though actually submitted two years earlier—contains the first appearance of the word "oxygène" [32]. The term "air vital" did not come until later. Lavoisier made his great attack on the phlogiston theory in a paper read in 1783 and published in 1786 [33]. He pointed out that the known facts could be explained as satisfactorily without the help of phlogiston as with it, and that therefore, on the principle of Occam's razor, it was probable that it did not exist. The theory was an error disastrous to the development of chemistry. The paper contains no new facts, but it is one of the most brilliant exhibitions of analytical reasoning which has ever been written. Macquer in his *Dictionnaire* had attempted to retain the facts and to fit the phlogiston theory to them, but Lavoisier showed that in all the arguments "phlogiston" was usually applied to two contradictory properties. It is notable that in one section [34] he refers to the changed conditions during the slow combustion of a metal— an example of the beginnings of his line of thought on respiration. As he says, physicists and geometers were then already abandoning the theory, but most of the chemists were still supporting it. This memoir was the beginning of the gradual disappearance of this famous theory.

The history of the discovery of the composition of water concerns us here only indirectly. McKie [35] in particular has recently disentangled the web of contradictory evidence. Lavoisier invariably gave full credit in his papers to the work of the British chemists, but for once he failed here to acknowledge his indebtedness to others. In June 1783 Lavoisier learned from Blagden what Cavendish had done. On June 24, in the presence of Blagden and others, he and Laplace made a rough experiment, and on the following day he took the precipitate step of reporting to the Academy that with Laplace he had synthesized a quantity of pure water; the report does not mention Cavendish. The careful results of Cavendish were not published until 1784. Meanwhile, on November 12, 1783, Lavoisier read a paper to the Academy which was published elsewhere in the following month [36]. The paper was then revised and was finally published in the *Mémoires de l'Académie* in 1784—*not* in the volume for 1783, but in that for 1781 [37]. Although Lavoisier cannot claim to be the discoverer of the composition of water, he was the first to explain the facts. Cavendish could not explain them correctly, since he was a confirmed phlogistonist. He thought water came from the two gases by deposition, and he did not realize that it was a compound. Indeed Lavoisier was one of the few at that time who *could* have explained the facts correctly.

The language of chemistry was still alchemical and iatro-chemical in nature, and from 1782 onwards three other chemists—de Morveau, Fourcroy and Berthollet—collaborated with Lavoisier in drawing up a nomenclature which would be in accordance with the

available. They show that Lavoisier had conceived the theory that whei. phosphorus and sulphur burned, the gain in weight was due to their combination with atmospheric air; he further suggested that the increase in weight in the calcination of metals was due to the same process. On February 20, 1773, he drew up a memorandum in his note-book. This is virtually a private programme of the experiments which he intended to carry out, his reasons for doing so, and a statement of what he hoped to discover. He says definitely that he intends to carry out a long series of experiments on the elastic fluids derived from any chemical changes. He feels that experiments must be performed to determine whether these elastic fluids are common air unaltered or modified in some way, or on the other hand whether they are emanations "of the minute and ultimate parts of substances". He recognizes that a vast number of experiments will have to be performed, but "the importance of the end in view prompted me to undertake all this work, *which seemed to me destined to bring about a revolution in physics and in chemistry*" (italics mine). This must be one of the most confident and prophetic statements in the history of science. He finished his memorandum with these words: "The processes by which one can succeed in fixing air are: vegetation, *the respiration of animals*, combustion, in some conditions calcination, also some chemical changes. It is by these experiments that I feel bound to begin" [21] (italics mine). This very important memorandum shows that Lavoisier had already, at the age of 29 years, visualized the future progress of the *Révolution chimique*. He seems to have had his attention directed towards the study of gases mainly as a result of his immature experiments on sulphur and phosphorus noted above. There had been in France no interest in the study of elastic fluids; as he says in the Introduction to the *Opuscules*, this was essentially a subject which had received the attention of English, German and Dutch chemists [22]. It is fairly definite that Lavoisier must have read widely on this subject about the end of 1772 and the beginning of 1773. Indeed, he devotes nearly a half of his *Opuscules Physiques et Chimiques*, which was written in 1773, to a history of experiments on air.

A point of vital importance to the present investigation which is brought out by this memorandum is the fact that by February 1773, and probably by the end of 1772, Lavoisier had sensed that a study of the elastic fluids involved a study not only of combustion but of respiration, and that he had already decided to undertake experiments on respiration.

The experimental work for the *Opuscules* was carried out at high pressure in a space of about six months, and the work was submitted for the approval of the Academy on December 7, 1773. In the early experiments recorded (Chaps. I to IV) it is clear that he thought that the gas liberated by the action of acids on metals was the same as the gas used up in calcination, and that this was therefore fixed air. In the next chapter he describes his famous experiment on the heating of minium and powdered charcoal in a bell-jar over water [23]. He concluded that the gas formed arose neither from the minium nor the carbon, but from a union of the two. There followed the five deductions on which much of his later work is based. Although, as Meldrum [24] has pointed out, these are not unexceptionable, they indicate that Lavoisier saw that calcination does not continue indefinitely in a closed vessel, and that the process consists essentially of a union between the metal and the air. The next series of experiments deals with the combustion of phosphorus in a bell-jar; experiments 6, 7 and 8 in this series [25] are especially important. From them Lavoisier showed that whatever it was in the atmospheric air which combined with the phosphorus, it was not water vapour. His final words are that the substance which combines with the phosphorus is "either air itself, or another elastic fluid contained, in a certain proportion, in the air which we breathe". From his note-books we see the doubts which he had in his mind [26]. In February 1773 he suspected that the air in minium was not "fixed air". In July, however, he had reversed his opinion and had tried to re-create common air by adding fixed air to the residual air left after the burning of phosphorus.

The missing link in the chain was provided by Priestley's discovery of "dephlogisticated air". Priestley, with the discovery of a number of new "airs" already to his credit, had obtained this gas in November 1771, but he had not then recognized it as another new "air". On August 1, 1774, he obtained an "air" by heating *mercurius calcinatus per se* (now known as mercuric oxide) and recognized from his tests that it was extraordinarily vigorous as a supporter of combustion. Towards the end of the same month Priestley met Lavoisier and his circle at the latter's house at the Arsenal, and it is known [27] that he talked of the properties of his new gas. Priestley thought it might be the gas we now call nitrous oxide, but Lavoisier immediately perceived that this was the clue which he was seeking. It was not until March 1, 1775, that Priestley realized that his new "air" was respirable, and soon thereafter that it could be used

Early Work on Respiration

As an example of the theories on respiration which were held up to the time of Priestley and Lavoisier, we may summarize the views of von Haller, the great physiologist who died in 1777, the year in which the new theory of combustion was formulated, and in which Lavoisier read his first paper on respiration proper. Haller admitted that the reasons why animals cannot live in vitiated air were not clearly recognized. He discussed the view that the air itself, or something vital in it—the subtle aerial particles of Mayow—reaches the blood and acts chemically, but was inclined to reject it. However, he believed that air exists in all the humours of the body, and he thought that possibly something was derived from the respired air. He was unwilling to commit himself regarding the nature of this substance, and on the whole he believed that air plays the part of a cement holding together the earthy elements of the body [47]. So far as animal heat was concerned he was driven back to the theory of Stahl that it was due to the friction of the blood as it passed through the blood-vessels. He could not quite understand how this theory explained the constant temperature of the body.

In leading up to Lavoisier's experiments on respiration it should be recalled that in 1757 Black had recognized "fixed air" as a distinct gas which arose from the burning of charcoal. At first he thought that it constituted the irrespirable part of the atmosphere, but later, on the discovery of nitrogen by Rutherford in 1772, he changed his views. Meanwhile Priestley was intrigued by the possibility of re-creating common air from vitiated air. In 1771—the year in which he discovered oxygen without recognizing it—he thought that, since common air is necessary for the continuance of both plant and animal life, the effect on each would be the same. He wrote later of his experiment: "I own I had that expectation, when I first put a sprig of mint into a glass jar, standing inverted in a vessel of water: but when it had continued growing there for some months, I found that the air would neither extinguish a candle, nor was it at all inconvenient to a mouse, which I put into it. The plant was not affected any otherwise than was the necessary consequence of its confined situation" [48]. Later, in August 1771, he showed that the same applied to air in which a candle had burnt itself out, and that the effect did not take place with leaves of mint, but that a growing plant was necessary. These experiments were not published until 1775 [49]. In the meantime Priestley had been carrying out numerous observations on the properties of dephlogisticated air, as was mentioned previously.

At this period Lavoisier was drawn almost unconsciously into his earliest observations on the respirability of various gases. At that time the British chemists at least, if not the French chemists in general, had two tests which they used by rote on any unknown air. One was the use of a candle or taper; the other was a test with a small animal. In order to put his investigations in correct perspective I have in writing this section compared the notes which Lavoisier made in his journals with the text of the original memoirs. It has already been noted that in the brilliant memorandum which he wrote in his laboratory note-book on February 20, 1773, he showed his belief that air was fixed by respiration, and that the process deserved further investigation [20]. In March 1773 he wrote in his note-book: "The apparatus for testing the effect of air by means of animals has been ordered and is almost ready. . . . In experiments on animals do not forget the frog" [50]. It is clear therefore that at this early period he had in mind a broader investigation than the mere placing of an animal in a gas to see how it reacted. On July 3 of the same year he was investigating the reduction of minium by carbon and a rat was used to test the resulting gas [51]. This is probably one of the experiments described in the *Opuscules* in which he gave the first proof that the gas produced by reduction of calces with carbon was identical with fixed air; he says there that in his examination of the gas, sparrows, mice and rats which were placed in it perished immediately [52]. It will be remembered that the *Opuscules* were published in January 1774. In the same work he described how a lighted candle was instantly extinguished when plunged into air in which phosphorus had been burned; a bird placed in the same air could breathe easily for half a minute [53]. Boyle had already made the same observation a century earlier. Despite this Berthelot, in commenting on the original note of this experiment in Lavoisier's note-book, remarks that the result is evidently erroneous and due to some accidental admixture of air [54]. Had he been able to recognize the fact at that period, Lavoisier would have obtained from this experiment a clue to the role of increased carbon dioxide tension in producing a stimulatory effect on the respiratory process. At this time he attributed the death of animals in the gases given off by effervescing fluids to the fact that these gases were easily soluble in water, and therefore could not retain sufficient tension to expand the lungs [55]. Thus up to this point Lavoisier's knowledge was limited to the lethal effects of certain concentrations of "fixed air". He had no idea of the function of the air which was inspired.

known facts. Lavoisier was chosen to introduce the system to the world of science, and this he did at a public session of the Academy on April 18, 1787. The details were given later by de Morveau, and the whole of the contributions by the four men were published in 1787 as the *Méthode de Nomenclature chimique*. The numerous names of chemical substances, which had been so picturesque and yet so unscientific, disappeared; in their place were established the names which we use to-day.

Lavoisier had no doubt realized for some time that the new theory of chemistry which he had created had rendered out of date all existing textbooks on the subject. An authoritative statement of the new chemistry was required, and this Lavoisier himself provided in 1789 in the *Traité élémentaire de Chimie* [38]. Even a short examination of this great work is beyond the scope of this paper, but a few remarks are necessary to determine Lavoisier's attitude to subjects which will be discussed later. In the first place, although he did not give any place to phlogiston, he reasoned that the matter of heat ("caloric") is a material substance and he included it in his table of elements. Next, he stated in his preface that he had imposed upon himself, as a law, never to advance but from what is known to what is unknown, and never to form any conclusion which was not an immediate consequence necessarily flowing from observation and experiment. He thus impressed upon all who read the book—and not merely on the fairly select body who read the *Mémoires de l'Académie*—the lines upon which chemistry was to develop in the future. Further, he made in it the first clear statement of the Law of Conservation of Mass as applicable to a chemical change. Finally, he applied Boyle's definition practically, and gave a table of the chemical elements, thirty-three in number. Apart from the inclusion of light and caloric among the elements the table marks a tremendous advance on anything which had gone before. The third part of the *Traité* was devoted to a description of the methods and apparatus used by Lavoisier. The illustrations of apparatus were drawn and signed by Mme. Lavoisier.

It remains only to mention briefly the importance of Lavoisier in the sphere of organic chemistry. Scheele had discovered a number of organic acids but organic analysis was hampered by the phlogiston theory and by a lack of understanding of the organic radicle [39]. As early as 1784 Lavoisier had determined the proportion of carbon in spirit-of-wine, in olive oil and in wax respectively by burning them in oxygen and absorbing the carbon dioxide in potash solution. (This paper was not published until 1787 [40].) The last of his extant laboratory note-books shows that in April 1788 he was working on the analysis of sugar by combustion with red oxide of mercury [41]. He later used oxide of manganese and chlorate of potash for the reduction, and he experimented on various resins and other organic substances. Dumas published in the *Œuvres* a previously unpublished Memoir of Lavoisier—no doubt incomplete—on his spirituous fermentation in which he sets out quite clearly the algebraic quality of an equation in organic analysis; he also indicated that vegetable substances must be regarded as a loose combination of oxygen, hydrogen and carbon, and that this combination can be easily upset by a medium degree of heat [42]. According to Dumas this paper probably dates from 1788. At this time Lavoisier must have been writing the *Traité*. In this he devotes chapters to the decomposition of organic substances by the action of fire, to vinous and acetous fermentation, and to putrefaction. Here again he stresses and illustrates the Law of Conservation of Matter [43]. We know, he says, that animal substances are composed of hydrogen, carbon, azote, phosphorus and sulphur, "all of which in a state of quintuple combination, are brought to the state of oxide by a larger or a smaller quantity of oxygen. We are, however, still unacquainted with the proportions in which these substances are combined, and must leave it to time to complete this part of chemical analysis, as it has already done with several others" [44]. Lavoisier had laid well and truly the foundations of organic analysis and a most important branch of physiology.

Before passing on to Lavoisier's work on respiration it might be well to emphasize that in the past much injustice has been done to his great British contemporary, Priestley. It used often to be said that Priestley was a brilliant experimenter with no theory except that of phlogiston behind his work. Even Meldrum [45] said that Lavoisier "was in earnest about what Priestley passed over lightly and amiably". Sir Philip Hartog [46, 9] has recently exploded this myth in brilliant fashion. He shows that many of Priestley's experiments exhibit constant planning, thought, and scientific imagination. To the end of his life he preserved a light-hearted suspicion of every hypothesis that seemed to him unverifiable, and the phlogiston theory was one of these hypotheses. His apparent adherence to the theory was not due to conservatism, and he remained a "sceptical chymist" to the last.

vitiated air, it was not enough merely to add the appropriate amount of eminently respirable air (as in his experiment on the burning of phosphorus); the existing chalky-acid must also be removed. He drew immediately the logical conclusion regarding the process of respiration. Either eminently respirable air is changed in the lungs to chalky-acid air; or an exchange takes place, the eminently respirable air being absorbed, and an almost equal volume of chalky-acid air being given up to the residual air from the lungs. To me the interesting point about this memoir is the fact that, while Lavoisier obviously favoured the change of eminently respirable air into chalky-acid air, he had to admit that there were strong grounds for believing that eminently respirable air did combine with the blood to produce the red colour. He gives full credit to Priestley for his observations on this point. Lavoisier does not seem to have realized, however, that it was not necessary that the chalky-acid which left the lung during one expiration should have been derived from the eminently respirable air which entered the lung *during the inspiration immediately preceding.* This is a small point, but it obviously proved a stumbling-block.

The Rubicon was apparently crossed the same year. At least, in the *Mémoires de l'Académie* for 1777 there appears an important memoir on combustion in general [63]. In this he propounds the false theory that all gases are compounds of solids or fluids with the matter of fire or of light. In combustion the "base of the air" combines with the burning substance, thus liberating its "solvent" as light and flame. In the combustion of sulphur and phosphorus this recombination takes place violently; in the calcination of metals, slowly. Then he puts forward the tentative hypothesis, which, however marred by errors it may appear to-day, is nevertheless a landmark in the history of physiology and in the development of his theory:

"Pure air"—that is, eminently respirable air, or oxygen—"in passing through the lung, suffers a decomposition analogous to that which takes place in the combustion of charcoal. Now, in the combustion of the latter, matter of fire is set free. Therefore, in the lung there must be in the interval between inspiration and expiration a similar liberation of matter of fire, and it is doubtless this which, carried by the blood throughout the animal economy, maintains there a constant heat of about 32½° Réaumur. This idea . . . rests on two constant and incontrovertible facts, namely: on the decomposition of the air in the lung and on the liberation of matter of heat which always accompanies the decomposition of pure air, that is, every change of pure air to fixed air." He points out that the only warm-blooded animals in Nature are those which breathe regularly, and he suggests that there is a constant relation between the heat of the animal and the quantity of air which is converted to fixed air in its lungs. This must have been speculative, and the influence of the phlogiston theory is still obvious in the passage which I have translated above.

It is of great interest to note that, although Lavoisier had now deduced by inference that the eminently respirable air which entered the lungs was involved in a chemical change by which heat was liberated, he was anchored to the idea that the change took place in the lungs in the interval between inspiration and expiration. In this change one factor was eminently respirable air; he did not know the nature of the other substance. Since in his view matter of heat was material—and was, as we have seen, one of his elements—it was perhaps not unnatural that he should conceive of it as being absorbed into the blood to raise the temperature of all parts of the body.

It is the duty of the historian to try to transport himself in spirit to the age which he is studying, and if we succeed in doing so now, Lavoisier's difficulties become less obscure. He had a fair idea that in respiration there was taking place in the body—or, as he thought, in the lung itself—a process analogous to slow combustion. The question which troubled Lavoisier was: Combustion of what? Combustion or even slow calcination involves a change which is not obviously for the better. A heap of red oxide of mercury would not be of much use to a maker of mirrors. The lung was evidently not consumed or altered by a process akin to calcination. Heat could not be liberated by eminently respirable air unless the latter acted with some other substance. The question before him now, therefore, was the nature of this other substance.

In 1778 Lavoisier was evidently pondering deeply on these subjects. At the beginning of the year he noted in his journal that Bucquet was carrying out experiments on asphyxia, and Lavoisier suggested that he should try marsh gas. A guinea-pig died in oxygen, and Bucquet did an autopsy [64].

The *Mémoires* for 1781 contain the important paper on the formation of the acid called fixed air [65], but this is not of great moment to the physiology of respiration.

The years 1775 and 1776 were very important in the development of Lavoisier's interest in the respiratory process. It has already been mentioned that, although Priestley had obtained a strange air in August 1774 it was not until March 1 of the following year that he had any idea of its respirability [56]. There followed a series of brilliant and exciting experiments in which Priestley not only shook his assumption that there could be no air better than common air, but that the new gas was actually four or five times better; later he obtained air which was five or six times better. By the time he published his second volume of *Experiments and Observations* in 1775 he had, by breathing the new air through a glass siphon, "reduced a large jar full of it to the standard of common air. The feeling of it to my lungs was not sensibly different from that of common air; but I fancied that my breast felt peculiarly light and easy for some time afterwards. Who can tell but that, in time, this pure air may become a fashionable article in luxury. Hitherto only two mice and myself have had the privilege of breathing it" [57]. Lavoisier's great debt to Priestley in putting him on the right track has already been noted. In the final version of his famous paper on the principle which combines with metals in calci-nation, Lavoisier says (1778) that this principle "is none other than the purest part of the air itself which surrounds us, which we breathe, and which passes, in this process, from a state of expansibility to one of solidity" [58]. He emphasized the fact that the whole of the air was not respirable, and to the purest part he gave the name "eminently respirable air". This final form of the memoir had evidently been modified by experiments which he had carried out in the meantime. His note-books show that from October 13 to 15, 1776, he carried out tests on the respiration of birds in dephlogisticated air. A red-breast lived for one hour in common air; another lived for three hours in dephlo-gisticated air, and a third, introduced into the air in which the second had died, lived for an hour. It is very interesting to see from this note that he thought that the birds were suffocated in a little atmosphere of fixed air, over which there was an atmosphere more pure than common air [59]. In reading Lavoisier's papers on respiration, therefore, it should be remembered that the laws of diffusion of gases were not at all understood at this period. Towards the end of this year (1776) he wrote in his note-book: "It seems that respiration in absorbing air vitiates a part of it", and we may make a shrewd guess that for Lavoisier the emphasis in this sentence was on the suggestion that a particular constituent part of the air suffered the alteration [60].

The first observation of 1777 which is of interest to us is contained in a memoir on the combustion of phosphorus. Lavoisier showed that when the combustion went on to extinction in the confined space of a bell-jar over water, the air which was left differed from common air; it was inert and he designated it *mofette atmosphérique*. If to this *mofette* he added the correct amount of dephlogisticated air which had been derived from a calx of lead or mercury, the residual air again became respirable, and the process of combustion could be repeated in it. Although in practice he had to add a little more dephlogisticated air—owing to the fact that it was seldom obtained quite pure—than the quantity of the air absorbed, he nevertheless found that the reaction was so definite that the amount of dephlogisticated air to be added could be calculated in advance [61].

Lavoisier had now reached the stage of realizing that the air of the atmosphere con-sisted of two parts, mixed in a definite proportion. One part was inert. The smaller and more active part was necessary for respiration and for animal life. This part was also necessary for the calcination—or combustion—of metals. No matter from what source the more active part was derived, it could be mixed in the proper proportion with the inert part to form common air. The relation may seem obvious to us, but it was a very different matter for Lavoisier. The assumption which we would make now involved *then* the rejection of the phlogiston theory. It was at this stage that he read a short memoir—*Experiments on the respiration of animals* [62]—which is of great importance in showing the manner in which his ideas developed. After a preliminary reference to Hales and Cigna, Lavoisier referred in generous terms to the ingenious, delicate and novel experiments of Priestley. He disagreed with Priestley's interpretation of the facts, and he proceeded to describe the experiments which had helped him in the development of his own theory. Lavoisier noted that there was a profound difference between the air in which a metal had been calcined and one which had served for respiration. Not only was the diminution of volume less in the latter; the respired air precipitated lime water, but the air after calcination did not. From this he deduced that there were two processes involved in respiration (*qu'il se compliquait dans la res-piration deux causes*), and that of these he probably knew only one. He therefore carried out another experiment by which he showed that about one-sixth of the volume of vitiated air consists of chalky-acid gas (*acide crayeux aériforme*). He had now thrown overboard the indefinite term "fixed air". Therefore, to re-create common air from

of heat and light standing in the way, and having to be disposed of in the convenient humours of the body. Later in the paper they give the first clear definition of the basal metabolic state. It is also noteworthy that they nowhere commit themselves any further regarding the substance with which vital air combines than that it is the *base* of fixed air.

These experiments seem to have been continued at intervals throughout the same year (1783). On May 5 Lavoisier tested the effect of dephlogisticated air, absorbed by nitrous acid, on sparrows. A week later he was observing the respiration of a guinea-pig in oxygen. On August 25 he was working on the specific weights of vital air, fixed air, and nitrous air. By December 22 he was investigating the heat produced by a guinea-pig [70]. In January 1784 he was using "apparatus A" to determine the caloric liberated by the respiration of birds [71]. About February 3 he was again working on the amount of carbonic acid liberated in the respiration of animals, and before March 16 he had weighed it [72]. Also in the winter of 1783-84 Lavoisier and Laplace made further extensive experiments on specific heats. These were not written up until 1793, and they were published posthumously many years later [73]. The paper contains nothing relevant to respiration.

In 1785 Lavoisier read to the *Société royale de médecine* a paper which carried his theory a stage further [74]. It contains what is, I think, the first clear statement in his memoirs that air is a mixture—although the evidence on which it is based rings strangely in our ears to-day. He then describes an experiment in which a guinea-pig was confined in a measured quantity of vital air for an hour and a quarter. At the end of this time there was a decrease in the volume of the vital air to the extent of about one thirty-secondth of its original volume, but the absolute weight of this air had increased. Hence, argued Lavoisier, the air breathed extracts something from the lung during respiration, and this substance when combined with vital air, forms carbonic acid. Only carbonaceous matter fulfils these conditions. By a calculation from the data Lavoisier then showed that in the experiment 52½ cubic *pouces* of vital air was used above the amount necessary to form the carbonic acid which was actually found. This additional quantity entered the lungs but did not come out in the same state. Either the oxygen combined with the blood, or with hydrogen to form water. He preferred the latter theory, and he calculated the amount of hydrogen which must have been used and the quantity of water formed. The same experiment was repeated in common air, though perhaps less satisfactorily. In this memoir Lavoisier gives the results of autopsies on asphyxiated guinea-pigs which were made by Bucquet. Now follows the significant observation that air which can be breathed easily must consist of about 25 parts of vital air to 75 of azote—variations either way are of importance; "but the ill-effects which animals experience, long before they have used up all the vital air in the air which they breathe, are indications of the irritating nature of the carbonic acid which is formed". He probably did not conceive of the irritation in the sense in which we understand it, but the observation is nevertheless important. Lavoisier finally gives the results of experiments which he carried out in public halls and in the theatre at the Tuileries. His figures for the analyses show a definite increase of carbonic acid in the vitiated air; and it is therefore not unexpected that he attributed the effects of vitiated air to this gas. No one seems to have observed previously that in this concluding section he made the observation that in a large audience each individual must breathe air which has passed a number of times through the lungs of others. This air must be charged with putrid exhalations. Is it possible, he says, that these may differ in youth and in age, in sickness or in health?

The Last Memoirs on Respiration and Transpiration

It was not until four more years had passed that Lavoisier read another paper dealing with respiration, and meanwhile he had taken as an assistant and collaborator a young man named Armand Seguin. Seguin is usually described as a physiologist in books dealing with Lavoisier. This *First memoir on the respiration of animals* was read on November 13 (or 17), 1789 [75], but it was not published until 1793. This is undoubtedly his greatest work on respiration.

The opening of the memoir emphasizes the known facts regarding the composition of air, and that the results depended upon exact analyses of gases carried out by Seguin's eudiometer method. From the emphasis which is placed on "liberation of caloric" it seems to me that his whole approach to the problem of respiration may have depended upon the fundamental observation that the heat of the body is maintained under very varied conditions. The first experiments were made on guinea-pigs. Having shown in his previous memoir that carbonic acid gas is noxious, it had to be removed from the gas or air breathed. The observations were made on a guinea-pig in a bell-jar

In it Lavoisier defined the *principe oxygine*, and fixed air or chalky-acid air he proposed henceforth to designate under the name of "carbonic acid". The memoir also contains the term *vital air*. He gives quantitative results of his experiments on the reduction of minium by charcoal, and he allows for the formation of water by the combustion of "inflammable air" in the charcoal. This observation is accounted for by the fact that the paper must have been revised in the light of Cavendish's water experiments, since it was not actually published until 1784.

While all these experiments were going on Lavoisier had been pursuing work on an important parallel line. In November 1777 he had begun to measure specific heats of various substances. These were interrupted, and taken up again briefly in 1781. In July 1782 the experiments began again [66]. He had, however, now obtained the collaboration of a scientist whose reputation stands as high as his own—Laplace, the mathematician. In the winter of 1782-83 very important work was carried out, and the *Memoir on heat* [67] was published in 1784, but in the volume of the *Mémoires* for 1780. Black was reputed to have used a calorimeter—but *not* an ice-calorimeter—a number of years previously, and Crawford was working on the subject of animal heat about the same time as Lavoisier; but these results do not affect the investigation which will now be described. Of the two men it was probably Lavoisier himself who invented a new type of calorimeter, of which examples were to be seen before the war in the *Conservatoire des Arts et Métiers* at Paris. The apparatus was based on the theory that if a warm body is applied to a block of ice, the heat first transforms a slice of ice into water, the remainder of the block remaining at the same temperature. If it were possible to obtain a hollow sphere of ice, the warmer atmosphere would act only on the outside layer, and the temperature of the remainder would be constant. If a warm body was then placed inside the hollow of the sphere, the inside layer of ice would be melted, but the temperature of the inner portion of the wall would be unaffected. Hence the water which collected inside the hollow would be due only to the cooling of the body inside it. The construction of the calorimeter will be understood from Mme. Lavoisier's illustration, which appeared in the original memoir and also in the *Traité*. The body to be investigated is placed in the wire basket. The wall of the sphere is represented by the middle chamber, filled with ice; the water produced is run off through the lower outlet. The middle chamber is itself insulated by the ice in the outer chamber. This long memoir contains many important observations, theoretical and experimental, but it is only the fourth, concluding, section which concerns us. The authors pointed out that recent experiments—those of Lavoisier of course—had shown that in respiration the vital part of the air is "either absorbed, or altered, or converted into fixed air by the addition of a principle which we shall call the *base of fixed air*, to avoid all discussion of its nature" (italics in the original) [68]. They then carried out experiments on the respirations of guinea-pigs in a confined atmosphere. From the average of their results they concluded that a guinea-pig produces 224 gr. of fixed air in ten hours, and by a variation of the method they showed that the changing of vital air into fixed air is the *only* effect of respiration on air. In experiments described earlier in the memoir they had shown that in the combustion of charcoal the production of one ounce of fixed air involves the melting of 26·692 oz. of ice. Hence the formation of 224 gr. of fixed air involves the production of heat sufficient to melt 10·38 oz. of ice. In an actual experiment with a guinea-pig in the calorimeter they found that in ten hours 13 oz. of ice were melted, and they thought that this represented approximately the heat which had to be renewed by the vital functions of the animal. For reasons which to us are not entirely satisfactory they also thought that this amount would have to be reduced by 2½ oz. to give an approximately true result. Hence, from the correspondence between the amount of ice melted by a guinea-pig and by the combustion of charcoal in the production of a given amount of fixed air in each case, they concluded that the principal cause of animal heat is that heat which is liberated in the transformation of vital into fixed air. They continue:

"Respiration is then a combustion, admittedly very slow, but nevertheless completely analogous to that of charcoal; it takes place in the interior of the lungs, without liberation of perceptible light, because the matter of fire is no sooner liberated than it is absorbed by the humidity (*humidité*; ? humours) of these organs. The heat which is produced in this combustion is transmitted to the blood which passes through the lungs and from there it courses through the whole animal system" [69].

Lavoisier and Laplace almost gave the true explanation; but just as the phlogiston theory had misled so many brilliant chemists, here was the theory of the material nature

remains·approximately constant. He also enunciated two laws which have apparently not been much followed up since then: that the increase in the pulse-rate is directly proportional to the work done; and that the oxygen consumed is proportional to the product of the respiration- and pulse-rates. In the memoir Lavoisier goes too far in saying that the absolute result must vary in individuals with such conditions as their age and state of vigour—since there is no evidence that Seguin was not the only subject. He gave 1,728 cubic *pouces* (34·0 litres) as an "average" figure of oxygen consumption for a man per hour, and he also gave provisional figures for the carbonic acid liberated, and the amount of carbon and hydrogen taken from the blood. Finally, he discussed what he considered to be the medical bearings of his discoveries. The statement is often made that Lavoisier held that the place where the slow combustion takes place is the lungs. A passage in this memoir makes one wonder whether he had not by this time a fairly open mind on the subject. He says that there is no decisive proof that the carbonic acid exhaled is produced in the lung or in the course of the circulation; it is even possible that this gas may be the product of digestion, may be carried to the lung, and liberated from the blood in proportion as the oxygen combines with it *by a superior affinity*.

The *First Memoir on Transpiration* [78] was read on April 14, 1790, but was not actually published until four years after his death. Transpiration is an aqueous emanation which exudes from the skin and from the lungs, and which is sensible only when it ceases to be in solution. Lavoisier approached the problem from the aspect of loss of weight in the individual. He conceived that the lung secreted "carbonized hydrogen"— from the *Traité* it would seem that this was his idea of the hydrocarbon radicle—and that the water formed from this and from the union of hydrogen and oxygen had to be got rid of. Seguin was equipped with a suit fitting close to the skin and made of a material similar to oiled-silk. In this way they were able to ascertain the loss of weight in the test individual due to respiration together with transpiration, and separately the loss due to respiration alone. Lavoisier estimated a man's loss of weight in twenty-four hours as 1 *livre* 13 *onces*.

A letter which Lavoisier wrote to Black of Edinburgh on November 13, 1790 [79], is his last authentic and untouched account of his views on respiration. He repeats the conclusions expressed in his first respiration memoir, and emphasizes that animal heat is constant in all circumstances, that respiration is the same in any concentration of oxygen provided that the carbonic acid is removed, and that nitrogen plays no part in the process. The results are given, apparently with much greater detail—which on examination proves to be largely superficial—in the *Second Memoir on Respiration* [80]. This paper was one of several communications read to the Academy by Lavoisier between March 9, 1791, and February 21, 1792: all of these have been lost with the exception of this and the following memoir [81]. Neither of these saw the light until 1814, when they were published, perhaps altered, by Seguin. The work for this present memoir was carried out on guinea-pigs, and the results are stated in detail. But although many experiments were carried out, the presentation of the data leaves much to be desired. Among new points introduced are the statement of the itching effect of carbonic acid gas on the skin—throwing some light as it does on Lavoisier's views regarding the noxious effect when the gas is respired—and the observation that in any respirable air, oxygen in excess of that necessary for combustion is inert.

The *Second Memoir on Transpiration* was read to the Academy on February 21, 1792, and published by Seguin in 1814 [82]. They believe that the transpired material would block the pores of the skin were it not for a surface respiration which takes place on the skin. That being the case, there must be alteration of the air near the skin surface. This point was investigated by withdrawing specimens of air for analysis from within Seguin's elastic suit. The action of air in complicating transpiration *per se* was also excluded by weighing Seguin before and after he entered a bath, and by analysing the bath water. Loss of weight in water was in all circumstances less than that in air. This was explained by the assumption that the skin contained both absorbing (*inhalant*) and excretory (*exhalant*) vessels, and that in a bath the absorbing vessels took in a little water. Throughout this memoir too much emphasis is placed on the possibility of the individual being able to maintain his body temperature by muscular work. They finally attempted to apply their findings to everyday life, and especially to the effect of clothing on the metabolism.

A full discussion of these memoirs must be reserved for another place, but meanwhile comment should be made on certain points. Lavoisier was undoubtedly the real discoverer of the true functions of oxygen in combustion, and he extended his results in

over water. The animal rested on network covering an elevated wooden dish (*sébile*) which was filled with caustic alkali by siphonage, and a similar dish containing alkali floated on the surface of the water. Individual experiments sometimes lasted several days, and Lavoisier showed that whether the atmosphere is vital air or common air, the amount of vital air consumed is always the same. Nitrogen and hydrogen were unaffected by respiration, and no more carbon or hydrogen were consumed in vital air than in common air. The very significant observation was now made that guinea-pigs consumed more vital air during digestion, and likewise during movement.

They then extended their observations to man, and Seguin *insisted* that he should be the subject. The apparatus used was shown at the meeting of the Academy, but the promise given by Lavoisier that it would be described in a later memoir was never completely fulfilled. From the brief particulars actually given in a later paper and from Mme. Lavoisier's drawing (fig. 2) it would appear that Seguin breathed oxygen through

FIG. 2.—LAVOISIER IN HIS LABORATORY AT THE ARSENAL. AFTER A DRAWING by Mme. LAVOISIER. Lavoisier stands at the pneumatic trough. Seguin is the subject of an experiment on the respiration of a man at rest. Mme. Lavoisier is taking notes.

a mask which was in some manner stuck to the face (*se mastiquait sur la peau*). They emphasize that the experiments were carried out many times. The thermometer scale used was that of Réaumur. (It should be noted *passim* that very few references have ever done justice to these observations. Of the two longest known to me, Lusk [76] tabulates the results but does not name the scale; Aykroyd [77], in reproducing Lusk's table, assumes that the Centigrade scale was used.)

Lavoisier showed that a fasting man at rest at a temperature of 26° R. (32·5° C.) used up 1,210 cubic *pouces* (23·8 litres) of oxygen per hour. When the temperature was reduced to 12° R. (15° C.) the consumption rose to 1,344 cubic *pouces* (26·5 litres) per hour. During digestion at an unstated temperature, presumably 15° C., he used 1,800 to 1,900 cubic *pouces* (35 to 37 litres) per hour. After exercise during which he did the equivalent of raising a weight of 15 *livres* to a height of 613 *pieds* in fifteen minutes (10,531 foot pounds)—temperature unstated—the oxygen consumption rose to 3,200 cubic *pouces* (65 litres) per hour, and when approximately the same amount of work was carried out during digestion the intake again rose to 4,600 cubic *pouces* (90·5 litres). Though these results are remarkably accurate, it is of more importance that Lavoisier established—and recognized that he had established—the fact that the amount of oxygen absorbed depends upon the three factors, temperature, food and work. He noted that in all the experiments the temperature of the blood

remains·approximately constant. He also enunciated two laws which have apparently not been much followed up since then: that the increase in the pulse-rate is directly proportional to the work done; and that the oxygen consumed is proportional to the product of the respiration- and pulse-rates. In the memoir Lavoisier goes too far in saying that the absolute result must vary in individuals with such conditions as their age and state of vigour—since there is no evidence that Seguin was not the only subject. He gave 1,728 cubic *pouces* (34·0 litres) as an "average" figure of oxygen consumption for a man per hour, and he also gave provisional figures for the carbonic acid liberated, and the amount of carbon and hydrogen taken from the blood. Finally, he discussed what he considered to be the medical bearings of his discoveries. The statement is often made that Lavoisier held that the place where the slow combustion takes place is the lungs. A passage in this memoir makes one wonder whether he had not by this time a fairly open mind on the subject. He says that there is no decisive proof that the carbonic acid exhaled is produced in the lung or in the course of the circulation; it is even possible that this gas may be the product of digestion, may be carried to the lung, and liberated from the blood in proportion as the oxygen combines with it *by a superior affinity*.

The *First Memoir on Transpiration* [78] was read on April 14, 1790, but was not actually published until four years after his death. Transpiration is an aqueous emanation which exudes from the skin and from the lungs, and which is sensible only when it ceases to be in solution. Lavoisier approached the problem from the aspect of loss of weight in the individual. He conceived that the lung secreted "carbonized hydrogen"— from the *Traité* it would seem that this was his idea of the hydrocarbon radicle—and that the water formed from this and from the union of hydrogen and oxygen had to be got rid of. Seguin was equipped with a suit fitting close to the skin and made of a material similar to oiled-silk. In this way they were able to ascertain the loss of weight in the test individual due to respiration together with transpiration, and separately the loss due to respiration alone. Lavoisier estimated a man's loss of weight in twenty-four hours as 1 *livre* 13 *onces*.

A letter which Lavoisier wrote to Black of Edinburgh on November 13, 1790 [79], is his last authentic and untouched account of his views on respiration. He repeats the conclusions expressed in his first respiration memoir, and emphasizes that animal heat is constant in all circumstances, that respiration is the same in any concentration of oxygen provided that the carbonic acid is removed, and that nitrogen plays no part in the process. The results are given, apparently with much greater detail—which on examination proves to be largely superficial—in the *Second Memoir on Respiration* [80]. This paper was one of several communications read to the Academy by Lavoisier between March 9, 1791, and February 21, 1792; all of these have been lost with the exception of this and the following memoir [81]. Neither of these saw the light until 1814, when they were published, perhaps altered, by Seguin. The work for this present memoir was carried out on guinea-pigs, and the results are stated in detail. But although many experiments were carried out, the presentation of the data leaves much to be desired. Among new points introduced are the statement of the itching effect of carbonic acid gas on the skin—throwing some light as it does on Lavoisier's views regarding the noxious effect when the gas is respired—and the observation that in any respirable air, oxygen in excess of that necessary for combustion is inert.

The *Second Memoir on Transpiration* was read to the Academy on February 21, 1792, and published by Seguin in 1814 [82]. They believe that the transpired material would block the pores of the skin were it not for a surface respiration which takes place on the skin. That being the case, there must be alteration of the air near the skin surface. This point was investigated by withdrawing specimens of air for analysis from within Seguin's elastic suit. The action of air in complicating transpiration *per se* was also excluded by weighing Seguin before and after he entered a bath, and by analysing the bath water. Loss of weight in water was in all circumstances less than that in air. This was explained by the assumption that the skin contained both absorbing (*inhalant*) and excretory (*exhalant*) vessels, and that in a bath the absorbing vessels took in a little water. Throughout this memoir too much emphasis is placed on the possibility of the individual being able to maintain his body temperature by muscular work. They finally attempted to apply their findings to everyday life, and especially to the effect of clothing on the metabolism.

A full discussion of these memoirs must be reserved for another place, but meanwhile comment should be made on certain points. Lavoisier was undoubtedly the real dis-coverer of the true functions of oxygen in combustion, and he extended his results in

brilliant fashion to the process of respiration in animals and in man. As he says, "the torch of life is lighted at the moment when the infant draws his first breath, and is extinguished only on his death" [83]. His experiments on metabolism—if they are correctly expressed in these last memoirs—were no doubt circumscribed by the fact that he thought that combustion probably took place in the lungs; that free hydrogen, or at least the hydrogen base or radicle, was combusted to form water; and that he had no idea that food could be stored in the liver and other organs for future use. Yet there is reason to believe that he might have solved these problems had he been granted a longer life. It has already been noted that he admitted that the blood might contain carbonic acid, and he says in one memoir that they intended to carry out blood analysis and experiments on digestion [84]. It is at least conceivable that the penetrating mind of Lavoisier would have ultimately noticed that if hydrogen from the body is consumed in the lungs to form water, it is very unlikely that it can be breathed unaltered in respired air—a fact which he had already proved. Lavoisier's ideas were probably not fully worked out at the time of his death. Certainly the presentation of the results in these last memoirs is scarcely adequate, and it is particularly unfortunate that Berthelot found no laboratory note-books relating to this period [85]. So far as oxygen consumption was concerned Lavoisier was on his own ground, and a master. He chose to follow this up by experiments on the loss of weight in metabolism. Considering his earlier experiments on calorimetry, he might quite possibly have switched over to heat loss had he lived longer—and then our already great debt to him might have been even greater. The fact that he had not done so at the time of his death was probably due to the difficulty of constructing a calorimeter for human experiments.

Reference is sometimes made to the highly-coloured passages in these last memoirs in which Lavoisier visualizes metabolism experiments of the future and drags in comparisons of metabolism in the rich and in the poor. In my view these passages are of no great importance. It should be remembered that Lavoisier had always been interested in economic matters, and that the Revolution was afoot. The style is different from that of earlier memoirs, and Seguin may have been in part responsible. This supposition would not be inconsistent with his later history. Seguin was 21 years old when the *First Memoir on Respiration* was read. He consorted with Fourcroy, Berthollet and other scientists who had revolutionary sympathies. In the year of Lavoisier's death he had, at the age of 26, become one of the budding capitalists of the Revolution. He had evolved improved processes for making leather, had had tanneries 'built for him, and in a few years was a very rich man. In his later years he was a leading authority on banking and finance, and a well-known eccentric [86].

On internal evidence there appear to be grounds for the suggestion that Lavoisier was only in part responsible for these last memoirs as they remain in their published form. Perhaps he intended them only as interim communications to the Academy, to be added to, corrected and polished—as was his wont—at leisure. No doubt the thoughts expressed are his, and he probably directed most of the experiments; but Seguin or some other person possibly wrote down Lavoisier's observations, the results of the experiments in brief, and his deductions from them. To these apparently Seguin added the extraneous analogies which are scarcely like the products of Lavoisier's logical and practical mind. A possible exception is the *First Memoir on Respiration*, which, apart from the fact that the experimental results are not given in great detail, is clearly on a different plane. Two years after Lavoisier's death his wife quarrelled with Seguin over the publication of the *Mémoires de Chimie*. Grimaux [87] records that in his proposed preface to the work Seguin attributed to himself an equal share with Lavoisier in the conception of the project. Mme. Lavoisier was indignant at his presumption, and the project was abandoned until 1806, when she herself edited the only two volumes of the *Mémoires* which appeared. From a detailed study of the last memoirs on respiration and transpiration I have formed the tentative opinion that Seguin merely acted as an assistant, and that conception and execution were both the work of Lavoisier himself. His generous acknowledgments of Seguin's part constituted a step which Seguin himself seems to have known very well how to use in his ascent. Until I have completed my study of Seguin's own writings on other subjects, however, I must advance this view with a certain reserve.

The Last Years

The last few years of Lavoisier's life, when these memoirs on respiration and transpiration were being written, belong to the history of the French Revolution. In 1789 the hurriedly assembled States-General became the National Assembly. Lavoisier, a member of the 89 Club, was possibly not out of sympathy with some of the aims of the Revolution; but the *Ferme* was anathema to the nation in its new mood. In January 1791 he was

the object of a scurrilous attack by Marat, and in March the *Ferme* was suppressed by decree of the National Assembly. From that time Lavoisier threw himself with renewed vigour into the work of the Commission of Weights and Measures, and into a defence of the Academy against its enemies within itself and in political circles outside. His work on the Commission survives, but the Academy in its old form was suppressed in August 1793. Difficulties also arose over the *Régie des Poudres*, and on August 15, 1792, Lavoisier moved from the house at the Arsenal which he had occupied so happily for seventeen years. His cup was not yet full. Although the *Ferme* no longer existed, its former activities were very suspect, and accusations were being made—quite wrongly—against the former Farmers. The inquiries were very protracted, and on November 14, 1793, they were arrested. Lavoisier and the other accused persons, including his father-in-law, were imprisoned in the Prison of Port-Libre. There followed long delays, and attempts to obtain the release of the accused. On May 8, 1794, the trial took place—that trial at which the President, Coffinhal, declared: *"La République n'a pas besoin des savants, il faut que la justice suive son cours."* On the same day the great injustice was done. "Only a moment to cut off his head", said Lagrange, "and perhaps a hundred years before we see such another."

The Revolution had accomplished its most criminal act, and the science of respiration had to wait over forty years for its next forward step.

I am indebted to Professor Charles Singer and to Dr. Douglas McKie for reading the typescript of this paper.

The weights and measures used throughout are, unless otherwise stated, those of the pre-Revolutionary French system.

· BIBLIOGRAPHY

1 GRIMAUX, E. Lavoisier. 1743-1794. Paris, 1888.
2 Œuvres de Lavoisier. 6 vols. Paris, 1864-93.
3 BERTHELOT, (P. E.) M. La Révolution chimique—Lavoisier. Paris, 1890.
4 MELDRUM, A. N. The Eighteenth Century Revolution in Science—The First Phase. Calcutta, 1930.
5 COCHRANE, J. A. Lavoisier. London, 1931.
6 AYKROYD, W. R. Three Philosophers (Lavoisier, Priestley and Cavendish). London, 1935.
7 McKIE, D. Antoine Lavoisier. The Father of Modern Chemistry. London, 1935.
8 FRENCH, S. J. Torch and Crucible. The Life and Death of Antoine Lavoisier. Princeton : London, 1941.
9 HARTOG, Sir PHILIP. The Newer Views of Priestley and Lavoisier, *Annals of Science*, 1941, 5, 1-56.
10 LAVOISIER. Réflexions sur le phlogistique. *Mém. Acad. R. Sci.*, 1783, p. 505; Œuvres, t. 2, 623.
11 BOYLE, R. Essays on Effluviums. London, 1673; WHITE, J. H. The History of the Phlogiston Theory. London, 1932; McKIE, *op. cit.* [7], p. 63.
12 PATTERSON, T. S. *Isis*, 1931, 15, 47, 504. (This passage on p. 543.)
13 *See* PARTINGTON, J. R. A Short History of Chemistry. London, 1939, p. 88.
14 BLACK, J. De Humore Acido a Cibis orto, et Magnesia Alba. Edinburgh, 1754; *see also* Alembic Club Reprint, No. 1. My reference is to the English edition of 1756, which is more important, in "Experiments and Observations," vol. 2.
15 LAVOISIER, in Méthode de Nomenclature chimique. Paris, 1787.
16 —— Analyse du Gypse; Œuvres, t. 3, 111.
17 —— Mémoires sur la Nature de l'Eau, &c., *Mém. Acad. R. Sci.*, 1770, pp. 73 and 90; Œuvres, t. 2, 1 and 11.
18 —— Œuvres, t. 2, 38.
19 GRIMAUX, *op. cit.* [1], p. 103.
20 MELDRUM, A. N. Archeion, 1932, 14, 15, 19.
21 Original in Berthelot, pp. 46-49. The translation used in quotation is by Meldrum, 1930 (*op. cit.* [4], pp. 8-10).
22 LAVOISIER. Opuscules Physiques et Chimiques; Œuvres, t. 1, 445.
23 —— Opuscules Physiques et Chimiques, Part II, Chap. V; Œuvres, t. 1, 598.
24 MELDRUM, *op. cit.* [4], p. 24.
25 LAVOISIER. Opuscules; Œuvres, t. 1, 646-49.
26 BERTHELOT, *op. cit.* [3], pp. 234-50.
27 PRIESTLEY, J. Experiments and Observations on Different Kinds of Air. London, 1 (1774), 2 (1775), and 3 (1777). My page references here and later are to my own copies: 1 (2nd edit., 1775); 2 (1st edit., 1775); and 3 (1st edit., 1777). For the Paris visit, see especially 2, 36 *et seq.* and 320. Cf. McKie, *op. cit.* [7], p. 161. For the early French attitude, *see* Grimaux, *op. cit.* [1], pp. 107-8.
28 LAVOISIER. Observations sur la Physique . . . de l'abbé Rozier, 1775, 5, 429.
29 McKIE, *op. cit.* [7], p. 203.
30 LAVOISIER. Mémoire sur la nature du principe qui se combine, &c., *Mém. Acad. R. Sci.*, 1775, p. 520; Œuvres, t. 2, 122.
31 —— Sur la combustion du phosphore de Kunkel, &c., *Mém. Acad. R. Sci.*, 1777, p. 65; Œuvres, t. 2, 139.
32 —— Considerations générales sur la nature des acides, &c., *Mém. Acad. R. Sci.*, 1778, 535; Œuvres, t. 2, 248.
33 —— *op. cit.* [10].
34 —— *op. cit.* [10], p. 647.
35 McKIE, *op. cit.* [7], p. 235 *et seq.*
36 LAVOISIER. Obs. . . . de l'abbé Rozier, 1783, 23, 452.
37 MEUSNIER and LAVOISIER. Mémoire ou l'on prouve par la décomposition de l'eau, &c., *Mém. Acad. R. Sci.*, 1781, 269; Œuvres, t. 2, 360.
38 LAVOISIER. Traité élémentaire de Chimie. Paris, 1789. In this study I have used the reprint from the 2nd edition (1789) in Œuvres, t. 1; also the 4th edition of Kerr's translation, Elements of Chemistry. Edinburgh, 1799.
39 For the early history of *organic* chemistry, *see* Partington, *op. cit.* [13], p. 216, *et seq.*
40 LAVOISIER. Mémoire sur la combinaison du principe oxygène avec l'esprit de vin., &c., *Mém. Acad. R. Sci.*, 1781, p. 593; Œuvres, t. 2, 586.
41 BERTHELOT, *op. cit* [3], pp. 306-10; DUMAS, in Œuvres, t. 3, 773.
42 DUMAS, *op. cit.* [41].
43 LAVOISIER. Traité; Œuvres, t. 1, 101; KERR, *op. cit.* [38], p. 187.
44 —— Traité; Œuvres, t. 1, p.111; KERR, *op. cit.* [38], p. 202.

brilliant fashion to the process of respiration in animals and in man. As he says, "the torch of life is lighted at the moment when the infant draws his first breath, and is extinguished only on his death" [83]. His experiments on metabolism—if they are correctly expressed in these last memoirs—were no doubt circumscribed by the fact that he thought that combustion probably took place in the lungs; that free hydrogen, or at least the hydrogen base or radicle, was combusted to form water; and that he had no idea that food could be stored in the liver and other organs for future use. Yet there is reason to believe that he might have solved these problems had he been granted a longer life. It has already been noted that he admitted that the blood might contain carbonic acid, and he says in one memoir that they intended to carry out blood analysis and experiments on digestion [84]. It is at least conceivable that the penetrating mind of Lavoisier would have ultimately noticed that if hydrogen from the body is consumed in the lungs to form water, it is very unlikely that it can be breathed unaltered in respired air—a fact which he had already proved. Lavoisier's ideas were probably not fully worked out at the time of his death. Certainly the presentation of the results in these last memoirs is scarcely adequate, and it is particularly unfortunate that Berthelot found no laboratory note-books relating to this period [85]. So far as oxygen consumption was concerned Lavoisier was on his own ground, and a master. He chose to follow this up by experiments on the loss of weight in metabolism. Considering his earlier experiments on calorimetry, he might quite possibly have switched over to heat loss had he lived longer—and then our already great debt to him might have been even greater. The fact that he had not done so at the time of his death was probably due to the difficulty of constructing a calorimeter for human experiments.

Reference is sometimes made to the highly-coloured passages in these last memoirs in which Lavoisier visualizes metabolism experiments of the future and drags in comparisons of metabolism in the rich and in the poor. In my view these passages are of no great importance. It should be remembered that Lavoisier had always been interested in economic matters, and that the Revolution was afoot. The style is different from that of earlier memoirs, and Seguin may have been in part responsible. This supposition would not be inconsistent with his later history. Seguin was 21 years old when the *First Memoir on Respiration* was read. He consorted with Fourcroy, Berthollet and other scientists who had revolutionary sympathies. In the year of Lavoisier's death he had, at the age of 26, become one of the budding capitalists of the Revolution. He had evolved improved processes for making leather, had had tanneries built for him, and in a few years was a very rich man. In his later years he was a leading authority on banking and finance, and a well-known eccentric [86].

On internal evidence there appear to be grounds for the suggestion that Lavoisier was only in part responsible for these last memoirs as they remain in their published form. Perhaps he intended them only as interim communications to the Academy, to be added to, corrected and polished—as was his wont—at leisure. No doubt the thoughts expressed are his, and he probably directed most of the experiments; but Seguin or some other person possibly wrote down Lavoisier's observations, the results of the experiments in brief, and his deductions from them. To these apparently Seguin added the extraneous analogies which are scarcely like the products of Lavoisier's logical and practical mind. A possible exception is the *First Memoir on Respiration*, which, apart from the fact that the experimental results are not given in great detail, is clearly on a different plane. Two years after Lavoisier's death his wife quarrelled with Seguin over the publication of the *Mémoires de Chimie*. Grimaux [87] records that in his proposed preface to the work Seguin attributed to himself an equal share with Lavoisier in the conception of the project. Mme. Lavoisier was indignant at his presumption, and the project was abandoned until 1806, when she herself edited the only two volumes of the *Mémoires* which appeared. From a detailed study of the last memoirs on respiration and transpiration I have formed the tentative opinion that Seguin merely acted as an assistant, and that conception and execution were both the work of Lavoisier himself. His generous acknowledgments of Seguin's part constituted a step which Seguin himself seems to have known very well how to use in his ascent. Until I have completed my study of Seguin's own writings on other subjects, however, I must advance this view with a certain reserve.

The Last Years

The last few years of Lavoisier's life, when these memoirs on respiration and transpiration were being written, belong to the history of the French Revolution. In 1789 the hurriedly assembled States-General became the National Assembly. Lavoisier, a member of the 89 Club, was possibly not out of sympathy with some of the aims of the Revolution; but the *Ferme* was anathema to the nation in its new mood. In January 1791 he was

Section of Otology

President—T. B. JOBSON, M.D.

[*November* 5, 1943]

Audibility of the Radio Voice

PRESIDENT'S ADDRESS

By T. B. JOBSON, M.D.

THE audibility of the Radio Voice must be considered from two points of view: that of the broadcasters and that of the audience.

(1) Clear enunciation by the announcers goes a long way to help the deaf part of the audience; it also greatly adds to the comfort of those whose hearing capacity is good. One observes this in listening at the cinema. You hear every word spoken by actors such as Ralph Richardson, Herbert Marshall, or Aubrey Smith. You strain to catch the words of others who shall be nameless. Much of their speech is inaudible even to the non-deaf.

The only cure for this lack of audibility is in the teaching of elocution. Quite apart from broadcasting or acting, our everyday comfort would be greatly increased if people were taught to speak properly. I suggest that elocution should be a standard subject in our schools, for both boys and girls, and not an extra subject, as it is now.

(2) The audience consists of all types and conditions of men; the highly educated, the quick thinker, the poorly educated, the slow thinker, those with normal hearing, those with defective hearing, the young with quick reactions, the elderly with slight senile deafness and a time-lag in interpreting the sounds heard. Also, we must include a number of other nationals whose knowledge of English is not perfect.

The deaf audience varies, of course, from the slightly deaf to the totally deaf. It includes those deaf for high tones, as well as those whose hearing is deficient in the lower tones.

When the deaf person is listening to the Radio Voice, he has to listen harder. He often has to strain his listening power and develops fatigue. This applies very particularly to the middle-aged and old people. They have a time-lag in interpreting the sounds. Their reactions to sound are delayed. So it follows that if such a person is listening to a very rapid speaker, he gets behind in his hearing, misses a word, and so may lose the gist of the sentences. He has to start again and do his best to catch up. He then gets tired of listening and gives it up as a bad job. When such a person listens to a speaker who speaks at an optimum rate, with adequate pauses, he has no difficulty whatever in hearing every word without fatigue.

In a broadcast on the B.B.C. announcers, Mr. John Snagge alluded to the listening "fathers", who did not hear as well as they used to. They represent a large and, I think, very important section of the audience.

The problem of the deaf has been taken up mainly by the National Institute for the Deaf. Their principal care, however, is of the deaf and dumb, and those suffering from extreme degrees of deafness, whereas our problem is to investigate subtotal deafness, to find out the numbers of the partially deaf who listen to the Radio Voice.

It is difficult to obtain any exact statistics of the partially deaf. In a survey made by Laura Spelman for the Rockefeller Foundation, it was found that three million children in American schools were suffering from some degree of deafness—a surprising number. In this country, evidence goes to show that the incidence is not so high. The Annual Report for year 1930, of the Chief Medical Officer of the Board of Education, shows defective hearing in 6,859 out of 1,770,779 children examined. This is about 4 per thousand. Other investigators have found 6 to 8 per thousand.

The number of the deaf increases with age. The various causes of deafness continue to operate and reach their maximum in old age. Mr. Arthur Wells investigated this subject in 1937 (*Brit. med. J.*, 1937 (ii), 18). After patient inquiry, he estimated that one in six persons in England and Wales was defective in one or both ears. This means that over seven millions of our people are somewhat deaf. This is a very considerable proportion of our Radio audience, and deserves the attention of the B.B.C.

STATISTICAL REVIEW

From this short analysis of the Radio audience, it is clear that it includes a large number of people who are dependent for their Radio reception on the skill and care

45 MELDRUM, *op. cit.* [4], p. 60.
46 HARTOG, Sir PHILIP. *Journ. Chem. Soc.*, 1933, Pt. ii, 890-902.
46*a* —— *Nature*, 1933, **132**, 25-26.
47 FOSTER, Sir MICHAEL. Lectures on the History of Physiology. Cambridge, 1901, pp. 228-30.
48 PRIESTLEY, *op. cit.* [27], Expts. and Obs., **1**, p. 50.
49 —— *op. cit.* [27]. For his general views, *see* Expts. and Obs., **1**, p. 70 *et seq.*—especially p. 86.
50 BERTHELOT, *op. cit.* [3], p. 245.
51 —— *op. cit.* [3], p. 248.
52 LAVOISIER. Opuscules ; Œuvres, t. **1**, 625 *et seq.*
53 —— Opuscules ; Œuvres, t. **1**, p. 654.
54 BERTHELOT, *op. cit.* [3], p. 245.
55 LAVOISIER. Opuscules ; Œuvres, t. **1**, 626.
56 PRIESTLEY, *op. cit.* [27], **2**, p. 40.
57 —— *op. cit.* [27], **2**, p. 102.
58 LAVOISIER. Œuvres, t. **2**, 127.
59 BERTHELOT, *op. cit.* [3], p. 291.
60 —— *op. cit.* [3], p. 272.
61 LAVOISIER, *op. cit.* [31], p. 140 *et seq.*
62 —— Expériences sur la respiration des animaux, &c., *Mém. Acad. R. Sci.*, 1777, p. 185 ; Œuvres, t. **2** 174.
63 —— Mémoire sur la combustion en général, *Mém. Acad. R. Sci.*, 1777, p. 591 ; Œuvres, t. **2**, 225.
64 BERTHELOT, *op. cit.* [3], pp. 274-5.
65 LAVOISIER. Mémoire sur la formation de l'acide nommé air fixe, &c., *Mém. Acad. R. Sci.*, 1781, p. 448 ; Œuvres, t. **2**, 403.
66 BERTHELOT, *op. cit.* [3], p. 223.
67 LAVOISIER and de LAPLACE. Mémoire sur la chaleur, *Mém. Acad. R. Sci.*, 1780. p. 355 ; Œuvres, t. **2**, 283.
68 —— *op. cit.* [67.], p. 319.
69 —— *op. cit.* [67], p. 331.
70 BERTHELOT, *op. cit.* [3], p. 292.
71 —— *op. cit.* [3], p. 294.
72 —— *op. cit.* [3], p. 286.
73 de LAPLACE, P. S., and LAVOISIER, A. L. Mémoire contenant les expériences faites sur la chaleur, &c., *Mém. de Chimie de Lavoisier*, 1806, t. **1**, 121 ; Œuvres, t. **2**, 724.
74 LAVOISIER. Altérations qu'éprouve l'air respiré ; Œuvres, t. **2**, 676.
75 SEGUIN and LAVOISIER. Premier mémoire sur la respiration des animaux, *Mém. Acad. R. Sci.*, 1789, p. 185 ; Œuvres, t. **2**, 688. For date of reading of this memoir *see* Grimaux, *op. cit.* [1], p. 352, and Œuvres, t. **2**, 704 (first line of text).
76 LUSK, G. The Science of Nutrition. Philadelphia and London, 1928, p. 19 ; and Nutrition (Clio Medica). New York, 1933, p. 61.
77 AYKROYD, *op. cit.* [6], p. 109.
78 SEGUIN and LAVOISIER. Premier mémoire sur la transpiration des animaux, *Mém. Acad. R. Sci.*, 1790, p. 601 ; Œuvres, t. **2**, 704.
79 LAVOISIER. Letter to Black, *Rev. Scientif.*, 1887, February 12, p. 193.
80 LAVOISIER and SEGUIN, A. Second mémoire sur la respiration. *Ann. Chim.*, 1814, **91**, 518.
81 GRIMAUX, *op. cit.* [1], p. 356.
82 LAVOISIER and SEGUIN. Second mémoire sur la transpiration des animaux, *Ann. Chim.*, 1814, **90**, 5 ; Œuvres, t. **5**, 379.
83 LAVOISIER. Œuvres, t. **2**, 692.
84 —— *op. cit.* [83], p. 713.
85 BERTHELOT, *op. cit.* [3], p. 307.
86 La Grande Encyclopédie ; Larousse, 19th century ; Hoefer ; Michaud.
87 GRIMAUX, *op. cit.* [1], pp. 331-333.

Section of Otology

President—T. B. JOBSON, M.D.

[*November* 5, 1943]

Audibility of the Radio Voice

PRESIDENT'S ADDRESS

By T. B. JOBSON, M.D.

THE audibility of the Radio Voice must be considered from two points of view; that of the broadcasters and that of the audience.

(1) Clear enunciation by the announcers goes a long way to help the deaf part of the audience; it also greatly adds to the comfort of those whose hearing capacity is good. One observes this in listening at the cinema. You hear every word spoken by actors such as Ralph Richardson, Herbert Marshall, or Aubrey Smith. You strain to catch the words of others who shall be nameless. Much of their speech is inaudible even to the non-deaf.

The only cure for this lack of audibility is in the teaching of elocution. Quite apart from broadcasting or acting, our everyday comfort would be greatly increased if people were taught to speak properly. I suggest that elocution should be a standard subject in our schools, for both boys and girls, and not an extra subject, as it is now.

(2) The audience consists of all types and conditions of men; the highly educated, the quick thinker, the poorly educated, the slow thinker, those with normal hearing, those with defective hearing, the young with quick reactions, the elderly with slight senile deafness and a time-lag in interpreting the sounds heard. Also, we must include a number of other nationals whose knowledge of English is not perfect.

The deaf audience varies, of course, from the slightly deaf to the totally deaf. It includes those deaf for high tones, as well as those whose hearing is deficient in the lower tones.

When the deaf person is listening to the Radio Voice, he has to listen harder. He often has to strain his listening power and develops fatigue. This applies very particularly to the middle-aged and old people. They have a time-lag in interpreting the sounds. Their reactions to sound are delayed. So it follows that if such a person is listening to a very rapid speaker, he gets behind in his hearing, misses a word, and so may lose the gist of the sentences. He has to start again and do his best to catch up. He then gets tired of listening and gives it up as a bad job. When such a person listens to a speaker who speaks at an optimum rate, with adequate pauses, he has no difficulty whatever in hearing every word without fatigue.

In a broadcast on the B.B.C. announcers, Mr. John Snagge alluded to the listening "fathers", who did not hear as well as they used to. They represent a large and, I think, very important section of the audience.

The problem of the deaf has been taken up mainly by the National Institute for the Deaf. Their principal care, however, is of the deaf and dumb, and those suffering from extreme degrees of deafness, whereas our problem is to investigate subtotal deafness, to find out the numbers of the partially deaf who listen to the Radio Voice.

It is difficult to obtain any exact statistics of the partially deaf. In a survey made by Laura Spelman for the Rockefeller Foundation, it was found that three million children in American schools were suffering from some degree of deafness—a surprising number. In this country, evidence goes to show that the incidence is not so high. The Annual Report for year 1930, of the Chief Medical Officer of the Board of Education, shows defective hearing in 6,859 out of 1,770,779 children examined. This is about 4 per thousand. Other investigators have found 6 to 8 per thousand.

The number of the deaf increases with age. The various causes of deafness continue to operate and reach their maximum in old age. Mr. Arthur Wells investigated this subject in 1937 (*Brit. med. J.*, 1937 (ii), 18). After patient inquiry, he estimated that one in six persons in England and Wales was defective in one or both ears. This means that over seven millions of our people are somewhat deaf. This is a very considerable proportion of our Radio audience, and deserves the attention of the B.B.C.

STATISTICAL REVIEW

From this short analysis of the Radio audience, it is clear that it includes a large number of people who are dependent for their Radio reception on the skill and care

of those who are issuing the broadcasts. · Not all of this number listen in, as it includes the very young, but it does include a very important group, namely, the elderly, who, in addition to their aural defect, develop a time-lag.· They hear the sound, but their cerebration is slow. They take longer to analyse and register the sound. This compels them to listen more intently, and, after a time, this produces fatigue. The speed at which the broadcast is uttered, and the adequacy of the pauses between the sentences, is of extreme importance in producing comfortable reception and interpreting the sounds, heard.

Senile deafness is composed of two factors: (1) Loss of acuity in hearing sound. (2) Delayed interpretation of the sound heard.

It is well known that hearing acuity diminishes with age. This diminution shows itself in the higher tones even at the age of 30. At ages over 50, the diminution for tones over 1,000 is marked. But even for tones in the speech range (128–512), acuity is lessened. At 60, the diminution is more marked (fig. 1).
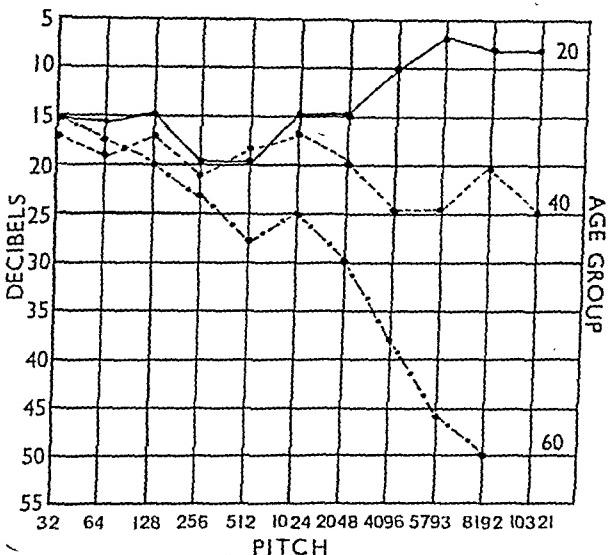
Graph showing loss of high tones with increasing age.
FIG. 1.—(Adapted from " Age Variations in Auditory Acuity ", by C. C. Bunch, *Archives of Otolaryngology*, 1929, 9, 625.)

This subject has been investigated by Dr. Bunch at the Johns Hopkins University. Fig. 1 shows very clearly the variation of hearing with age. It must be borne in mind that these tests were done on people who made no complaint of deafness. They do not include those whose deafness had become manifest.

We are concerned at the moment with the loss of hearing for the human voice— tones C.128 to C.512. The diagram (fig. 2) (Negus, V. E., "Mechanism of the Larynx",
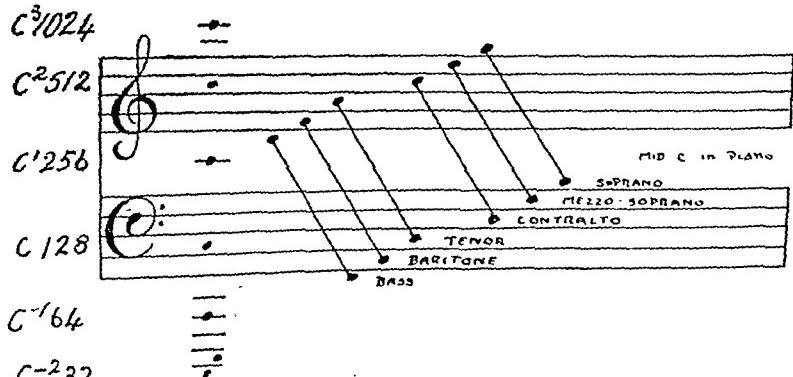
FIG. 2.—Diagram showing range of *the normal* human singing voice. (Adapted from diagram by V. E. Negus, in "Mechanism of the Larynx", p. 432, fig. 151.)

page 432, fig. 151, Heinemann, 1929) explains this point very clearly. It shows that the highest note in the average female voice is only midway between C.512 and C.1024, and the lowest bass note in the average male is midway between C.64 and C.128. The fundamental tones of the ordinary speaking voice lie between these extremes.

The second factor in senile deafness is delayed hearing, the slowing-up of the interpretation of the sounds heard, or delayed cerebration. The audiometer does not measure this factor. Even our consulting-room testing, by watch, whisper, and conversational voice, does not demonstrate this. A patient will often hear a whisper at 10 or 12 feet, and yet fail to understand a person who is talking rapidly, even in a louder voice. This combination of diminished hearing with delayed hearing exists in a large proportion of the Radio audience. This group must be added to that of the estimated one-sixth who show actual evidence of deafness.

The time-lag is a very important point. It increases gradually with age. Let us assume that it begins to manifest itself about the age of 50. The Registrar-General's figures for 1938 give the "over 50" (i.e. 50 to 85 years old and upwards) number of our population as 10,289,800. No doubt a large proportion of these are keen listeners to the B.B.C.

There are also a large number of foreigners here at present. They too have a lag unless they are very expert linguists.

All credit must be given to the B.B.C. for the trouble and care they take in making their broadcasts. The announcers are for the most part excellent. It is difficult to enforce a certain rate of speech and a certain space of time for pause, but I do think one should try to find an optimum rate, a rate that would not be tedious to the quick hearers, and yet acceptable to the deaf. The broadcaster is here in a dilemma. He has an audience of millions. He has to do his best to please everybody. Some of his deaf listeners, the early otosclerotics, and those with middle-ear deafness, hear the higher tones better. They hear the voices of children and females better than men. However, the number of people with this type of defect is much less than those who belong to the older group, who hear lower tones better.

My deaf patients say they can hear every word of Mr. Churchill's speeches, but hardly a word of some of our popular comedians.

The larger proportion of the deaf audience hear a man's voice more easily than that of a woman. Even the golden voice of the lady-announcer fails to charm. A man is certainly the best choice for a Radio speaker, but even he, if he wishes to reach the maximum number of his audience, must carefully arrange, not only his elocution, but also his rate of speech and his pauses. Of course one realizes that the slow, stately oratorical style is apt to be tedious to the majority of his audience who have no hearing defect, but I do think that there is an optimum rate of speech, which, combined with adequate pauses, would give untold comfort to the deaf portion of his audience. It should be possible to ascertain this optimum rate of speech and thus bring comfort and enjoyment to millions.

Mr. John Snagge: We of the B.B.C. are not unaware of our responsibilities in the matter of the spoken word. But it must be remembered that the microphone is a new invention and "broadcasting" was an unknown word in the days of my own grandfather. Our age is 21. In ten days time the B.B.C. "comes of age". In those twenty-one years we have had to find our way, and we have learned a lot, but we have not, and shall not have learned all there is to know for many years to come. Indeed, I have spent during those twenty-one years only nineteen years in company with the microphone, and I can say with truth that the problems of to-day are far greater than ever they have been, and I believe sometimes that the longer I spend in broadcasting the less I know.

In the matter of medical science I am a layman. The only training I have received in broadcasting comes from, probably the finest school of all, *experience*.

What I may say about the Radio Voice must apply only to the work which is being done by the announcers, news readers, and those people who are selected and appointed to the B.B.C. to be the official voice, or if you will, the "shop window" of the B.B.C. We cannot any more than anyone else give people new voices. We have not the time, at any rate just now, to be the Professor Higgins of Bernard Shaw's "Pygmalion". So far as the spoken word and English of the announcers is concerned, we are not there to instruct our listeners. We are there to be understood by the greatest majority of listeners. Criticism is often justified, and if constructive is often invaluable. It is by this means that we have learned to find our way, and very largely why the B.B.C. does to-day hold a good deal of respect both in this country, and, in these days of war, throughout the world.

The President's plea for the deaf is one of which we are not unconscious, and indeed I have myself learned much which I only hope may lead to a better service to them. But they are not our only problem. What of those who do not speak the English of the South, of those who speak and whose ears are attuned to the many dialects and hundreds of near dialect and accent speech in which we abound? Is our audience the individual sitting before his fire in his own home, or the one who is listening to a public loudspeaker with scores of others, or maybe the one who is trying to hear in a crowded and noisy canteen or the mess deck of a ship at sea?

And what of the quality of reception due either to bad reception areas or poor quality receiving sets?

I would like, if I may, to say a word about the most obvious and best known of our activities so far as Home Listeners are concerned—that of the news bulletins and their reading. To paraphrase a famous advertisement, they should be read "Not too slow, not too fast, but just right". What is "just right"? There are many factors which combine to make audibility and intelligibility. The President spoke of enunciation. This must be one of the most important factors, but it can be overdone, and when it is the all-important rhythm of English may be lost. It is, I think, a national failing that we are lazy speakers of our language. We do not as a whole move our mouths properly when we speak. Compare us with some foreigners such as the French or the Italians. We have a habit of slurring our words and sentences, and I agree whole-heartedly with the President's suggestion that as a matter of course we should be taught to speak. We should be taught all those things that go to make for clarity of speech—emphasis, pausing, speed, intonation. I do not, however, suggest that a standard form of English should be spoken throughout the length and breadth of the country. Our true dialects should never be allowed to die; they are characteristics and traditions of which we may well be proud. But there are accents and intonations which are neither traditional nor pure, and which have crept into our speech, and which jar badly on the ear. But there must be, and I believe there is, a standard form of English which is understood by all, or nearly all, English-speaking people, and it is this form which we in the Corporation have tried to maintain.

The microphone and loud speaker are not kind. They tell the truth sometimes unpleasantly. There are many that I know, and I can speak personally, who when they first heard a recording of their own voice were surprised and often shocked.

We must always bear in mind that affectations or simple curiosities of speech which would not normally be noticed in physical conversation may cause continual irritations when heard through the loud speaker, and they are often emphasized. Once a voice irritates, the listener is distracted 'from the sense of the words or speech, and will often say that he cannot *hear* the speaker. In point of fact he is not listening.

There was a curious and interesting incident about the speed of reading which came to light a year or so ago. We were told by letter, telephone and verbally that the midnight news was always read much too fast. Many people added that no doubt the news reader wished to go to bed, but that night was the only chance he or she had to listen, as they worked all day and late. The accusations became so general that I investigated the facts.

It was found in fact that there was no alteration at all in the speed of reading. What was, I think, the answer was that the reaction of the listener at that time of night, and after long hours of work, was slower. The fault did not lie with us, but the cure did. The midnight news is therefore so far as possible read just that fraction slower.

The broadcaster has to rely solely upon his voice—he cannot give meaning or clarity by gesture or expression as we do in our conversations. Therefore clarity of enunciation is of the first importance.

I have learned much from what the President has said regarding speed in relation to those whose misfortune it is to be deaf. I think there may well be a general optimum, but there is also an individual optimum. There can no more be a general optimum speech for all and any speaker than there is a general standard of language. The individual characteristics count greatly in accordance with the other factors which go to make for clarity. The speed in words per minute of those who read the news varies between 163 and 176 words per minute, but one is said by our listeners to be more audible than another. And not by any means the same reader; and certainly the most audible is not the slowest.

The secret of speed does not lie in words per minute, but in proper and adequate pauses and in realizing and transmitting the sense values of the English language. Here too rhythm plays an all-important part; a pause however brief, wrongly placed, can cause the listener uncertainty as to the meaning, and in adjusting himself thereby does not listen to the next few words.

The B.B.C. during its few years of existence has not only adopted a standard form of English with so far as possible a standard pronunciation, but has also developed and established a standard form of reading the news bulletins. We heard much at one time about the "tendentious inflection", implying that the reader was conveying his own interpretation of the news and failing to be impersonal; others complaining that he was so impersonal that he showed his disinterest in the news. He must be impersonal, not only in the political matters, but in all facts, news, and information, it is his job to convey. It is for the listener to give the interpretations.

During 1940 when the reading of news was not a particularly pleasant or enviable occupation (we broadcast day after day a series of setbacks and of defeats) it was no uncommon thing to receive letters from our listeners saying on the one hand: "I know the news is bad, why should the reader make it worse?" and on the other hand: "The news is bad, but don't let the reader put on forced cheerfulness." And both listeners would be referring to the same bulletin and both asking "Why can't we have someone to read the news whom we can hear?" What they really meant was "to whom we will listen". You may be quite sure that when it is good news these same people will, and do, listen regardless of the reader.

Twice recently an experiment was tried by introducing to the regular team a reader who brought with him inflections and traces of dialects not heard amongst news readers till then. One was from the North Country, another from Scotland. Both these men were good readers so far as tone, speed, emphasis, and phrasing were concerned. The experiment failed—failed that is from the general point of view. They had of course a full measure of appreciation from listeners in their own areas or county. It failed for two reasons. Firstly because they were different from the others and from each other, and therefore distracting. The short "a" was heard in words like "aircraft", "castle", and many were listening not to *what* he was saying but *how* he said it. In another case

the listeners complained that they never knew whether he was talking about Burma or a bomber, and once again we were told that *he couldn't be heard.*

The second reason is I think interesting. Both these men said the same thing. It was, they said, difficult for them to read the news as it was written and give full value to their form of speech. The idiom of the North and Scotland is quite different. The writing was Southern English and the voice Northern.

Many times we have been asked whether women will ever read the news, and if not why not. The answer is that it is not the intention of the B.B.C. to appoint women news readers at present. This is in no way a reflection on their ability to read aloud, but because there are many people whose feelings would be ruffled in hearing news descriptions of war and particularly of battles read by women, and there is also the additional reason that, as the President so rightly said, a man's voice is by many more easily heard than a woman's.

I hope I have been able to give some idea of the complexities which surround the life of the official broadcaster. It is a form of public speaking which is not comparable with any other. Recently we made an investigation into the speeds of speech of a number of people who broadcast. Figures taken, all over a period of three minutes, showed that the speeds of the professional broadcasters headed a list in a group. The fastest of the news readers showed the figure 528, the slowest 488.

The difference is almost entirely made up not by speed of words, but length of pauses. The average pausing between sentences in the first case being just under two seconds, and between items three seconds, and in the second case two seconds between sentences and over four between items. The clarity in both cases was excellent. The other readers all maintained the same average speed with the same average pausing. Commander Kimmins who has broadcast so admirably on Naval affairs showed a speed in this category—510 words over three minutes, but his average pausing shewed only 1½ second average.

The second group are taken from the ranks of public speakers. The Prime Minister, speaking over the microphone following the fall of France, averaged 400 words in three minutes with average two second pauses at end of sentences and 2½ at the end of paragraphs, and 1 to 1 4/5th in mid-sentence.

The Deputy Prime Minister's speed was also 400 words in three minutes and his pausing at the end of sentences slightly less than two seconds, but mid-sentence pausing the same.

The Archbishop of Canterbury, in broadcast address, was considerably slower, 325 in three minutes, but the pausing was considerably different. In mid-sentence or mid-phrase pauses were sometimes as great, if not greater, than at the end of a sentence or paragraph. This is a speech device frequently heard in the Church. Possibly it is the result of the spoken as opposed to the written word.

One further instance is, I think, interesting. In a studio broadcast the Foreign Secretary spoke 385 words in three minutes with average pausing. A broadcast speech from the Royal Albert Hall before a large audience, showed a rate of 100 words. Here surely is the reason why the public speaker when before the microphone shows a considerably lower speed. (The figure of 100 is, by the way, the figure excluding applause.) The public speaker can gauge his speed by his visual audience. He can, in a large hall, theatre, or church hear his own voice and hear perhaps the echo of it. The broadcaster cannot.

If the broadcaster were to speak as though he were before a large audience, as though, in fact, he were on a platform, the listeners would be the first to condemn.

No one wishes to have speeches made to him in his own home. He wishes to hear clearly, not loudly, intimately not pompously, or too formally, what the news or information is. Here lies the success of many broadcasters—C. H. Middleton, Christopher Stone, the late Professor John Hilton. It's not so much what they said as the way they said it. They used the language and phraseology of the ordinary man. Their speed, their pausing, their emphasizing, their tone, was normal in everyday speech and they could be heard.

The average receiving set does not give a true and faultless reproduction of the sound vowels and consonants as they leave the mouth. Much of it, when heard at the loudspeaker, must be guesswork. If the English is strange, the strain on the listener is greater and the greater the strain, the sooner the fatigue, until the listener gives up and complains he cannot hear.

We in the B.B.C. must remember that the listener should not have to strain to listen. That is why our Talks Department and our Presentation Department spend much time in editing and watching the scripts and announcements which are broadcast, so that what is said should be said in the simplest way and thereby understood and heard without strain or fatigue.

The President referred to some of the comedians who broadcast. Not all are transgressors in the matter of speed. How often do we hear a question asked by one and the question repeated by his companion and sometimes twice repeated before the answer and the joke is told! But there are others, I agree, who are fast and much of the success of Tommy Handley is his speed and the unexpectedness of his remarks. Take these away from him and his popularity would quickly die. I fear there may be a number who cannot listen through faulty hearing, but I do know cases of elderly people who do and can hear him because I think they enforce concentration.

But they are the artistes who come on occasions to the B.B.C. The regular broadcasters, and particularly the announcers, have many factors to bear in mind in front of the microphone, and they have, by experience, developed and practised a fairly consistent rate of speech. The optimum must, I think, be largely individual, the natural characteristic of the individual should be retained.

The great disadvantage of broadcasting is that it makes its appeal to one sense only. It is of the utmost importance that broadcasters should keep in mind the value of the beauty of speech. They must, in addition to regularizing their speech, modulate the voice as to pitch, emphasize correctly and be skilled in the subtle use of pauses so as to introduce the exact shade of colour required to keep up the interest and prevent any suggestion of boredom. And they must never forget that "father does not hear quite as well as he used to."

And what of the quality of reception due either to bad reception areas or poor quality receiving sets?

I would like, if I may, to say a word about the most obvious and best known of our activities so far as Home Listeners are concerned—that of the news bulletins and their reading. To paraphrase a famous advertisement, they should be read "Not too slow, not too fast, but just right". What is "just right"? There are many factors which combine to make audibility and intelligibility. The President spoke of enunciation. This must be one of the most important factors, but it can be overdone, and when it is the all-important rhythm of English may be lost. It is, I think, a national failing that we are lazy speakers of our language. We do not as a whole move our mouths properly when we speak. Compare us with some foreigners such as the French or the Italians. We have a habit of slurring our words and sentences, and I agree whole-heartedly with the President's suggestion that as a matter of course we should be taught to speak. We should be taught all those things that go to make for clarity of speech—emphasis, pausing, speed, intonation. I do not, however, suggest that a standard form of English should be spoken throughout the length and breadth of the country. Our true dialects should never be allowed to die; they are characteristics and traditions of which we may well be proud. But there are accents and intonations which are neither traditional nor pure, and which have crept into our speech, and which jar badly on the ear. But there must be, and I believe there is, a standard form of English which is understood by all, or nearly all, English-speaking people, and it is this form which we in the Corporation have tried to maintain.

The microphone and loud speaker are not kind. They tell the truth sometimes unpleasantly. There are many that I know, and I can speak personally, who when they first heard a recording of their own voice were surprised and often shocked.

We must always bear in mind that affectations or simple curiosities of speech which would not normally be noticed in physical conversation may cause continual irritations when heard through the loud speaker, and they are often emphasized. Once a voice irritates, the listener is distracted from the sense of the words or speech, and will often say that he cannot *hear* the speaker. In point of fact he is not listening.

There was a curious and interesting incident about the speed of reading which came to light a year or so ago. We were told by letter, telephone and verbally that the midnight news was always read much too fast. Many people added that no doubt the news reader wished to go to bed, but that night was the only chance he or she had to listen, as they worked all day and late. The accusations became so general that I investigated the facts.

It was found in fact that there was no alteration at all in the speed of reading. What was, I think, the answer was that the reaction of the listener at that time of night, and after long hours of work, was slower. The fault did not lie with us, but the cure did. The midnight news is therefore so far as possible read just that fraction slower.

The broadcaster has to rely solely upon his voice—he cannot give meaning or clarity by gesture or expression as we do in our conversations. Therefore clarity of enunciation is of the first importance.

I have learned much from what the President has said regarding speed in relation to those whose misfortune it is to be deaf. I think there may well be a general optimum, but there is also an individual optimum. There can no more be a general optimum speech for all and any speaker than there is a general standard of language. The individual characteristics count greatly in accordance with the other factors which go to make for clarity. The speed in words per minute of those who read the news varies between 163 and 176 words per minute, but one is said by our listeners to be more audible than another. And not by any means the same reader; and certainly the most audible is not the slowest.

The secret of speed does not lie in words per minute, but in proper and adequate pauses and in realizing and transmitting the sense values of the English language. Here too rhythm plays an all-important part; a pause however brief, wrongly placed, can cause the listener uncertainty as to the meaning, and in adjusting himself thereby does not listen to the next few words.

The B.B.C. during its few years of existence has not only adopted a standard form of English with so far as possible a standard pronunciation, but has also developed and established a standard form of reading the news bulletins. We heard much at one time about the "tendentious inflection", implying that the reader was conveying his own interpretation of the news and failing to be impersonal; others complaining that he was so impersonal that he showed his disinterest in the news. He must be impersonal, not only in the political matters, but in all facts, news, and information, it is his job to convey. It is for the listener to give the interpretations.

During 1940 when the reading of news was not a particularly pleasant or enviable occupation (we broadcast day after day a series of setbacks and of defeats) it was no uncommon thing to receive letters from our listeners saying on the one hand: "I know the news is bad, why should the reader make it worse?" and on the other hand: "The news is bad, but don't let the reader put on forced cheerfulness." And both listeners would be referring to the same bulletin and both asking "Why can't we have someone to read the news whom we can hear?" What they really meant was "to whom we will listen". You may be quite sure that when it is good news these same people will, and do, listen regardless of the reader.

Twice recently an experiment was tried by introducing to the regular team a reader who brought with him inflections and traces of dialects not heard amongst news readers till then. One was from the North Country, another from Scotland. Both these men were good readers so far as tone, speed, emphasis, and phrasing were concerned. The experiment failed—failed that is from the general point of view. They had of course a full measure of appreciation from listeners in their own areas or county. It failed for two reasons. Firstly because they were different from the others and from each other, and therefore distracting. The short "a" was heard in words like "aircraft", "castle", and many were listening not to *what* he was saying but *how* he said it. In another case

that the analysis of speech in a scientific fashion had not really begun. A few people had tried it, but they had not gone very far. A good deal could be done, for example, if one only heard one's own voice recorded back again, so that one perceived its faults. Oliver Wendell Holmes said that it would be an interesting thing to have a mirror for the voice, and suggested that it would be rather pleasant to have a replica of oneself with whom one could speak, getting inside him or outside him as the case might be. That would be rather a dull or perhaps painful existence. Yet Oliver Wendell Holmes realized that a speaker did not appreciate the sound of his own voice, and many people were shocked, as Mr. Snagge had said, when they heard it for the first time. Records might be taken of broadcasters and fired back at them for their criticism, though perhaps that was already done by the B.B.C.

One other investigation was the electrical recording of speech sounds and it could be done effectively by the cathode-ray oscillograph. This very sensitive ray gave a graph of the most rapid speech sounds which were then compared with other speech sounds. A colleague of the speaker's, Dr. Curry, began an inquiry of this kind just before the war, but was not able to continue it. He took records of Northumbrian dialect and compared it with standard English. The records were taken by the cathode-ray oscillograph showing the fluctuations of the beam of light, and the comparison between the two records was very striking. Speakers who used dialect gave a very different record from those who spoke what was known as standard English. He suggested that this matter should be worked out not merely by ear, so to speak, but scientifically by electrical recording methods.

Air Commodore E. D. D. Dickson (R.A.F.) said that in the R.A.F. they had facilities for teaching people how to speak correctly through the microphone from the point of view of operational requirements. Control Officers were taught the proper way to give instructions and orders, and gramophone records were made of their voices and played back to them to make them aware of their faults.

Mr. H. V. Forster said that in an effort to arouse the interest of the student to understand the mechanism of voice and speech, he had been grateful to be able to refer to Mr. Negus' well known comparative researches in the animal world. The voice of the ox was mellow because of the massive structure of the vocal cord. The voice of the parrot owed its quality to a well developed syrinx, but its remarkable powers of speech were due to the large and mobile tongue. The rigid beak would be a poor substitute however for the flexible lips and cheeks of man.

He would ask Mr. John Snagge to account for the popularity of the crooner. It had occurred to him that her success depended on clear diction, that of the legitimate singer on vocal instrumental effect rather than the listener's appreciation of the sung word.

Good diction relied on the clear enunciation of consonants. To confuse the numbers "five" and "nine" was common in telephone calls.

It was obvious that the "signal" language of the Armed Forces was designed to avoid such errors which might have serious consequences.

Mr. John Snagge, in reply, said that on the question of scientific investigation with the cathode ray, this had been a serious consideration with the B.B.C. and was taken up by them before the war. In wartime, however, they had not been able to get any further with it. Before the war they had had the help of the late Professor Lloyd James, an expert in phonetics, who was actually investigating with the cathode ray at the time the war broke out. The B.B.C. would eventually do something of that nature.

On the question of gramophone records of speech, this could be a very dangerous thing. The gramophone record of a man's own speech might shock him so much that he would be afraid to speak thereafter. He recalled an instance in the B.B.C. when a record was taken of the talk of a certain speaker and after he had finished a loudspeaker came on, repeating his speech from the record. This man listened for a minute or two, and then he said: "Who is that pompous ass who is reading my speech?" In fact, he could not tell whether anybody was going to be a good or a bad microphone personality by merely listening to them. Their speech had first to be recorded.

On the matter of of acoustics, the B.B.C. had done a great deal in this direction. The first step was carried out when they moved into Broadcasting House where the studios were specially designed, as they had not been at Savoy Hill, and various experiments were carried out in the matter of the lining of the walls. He did not himself think that to the listener it made a great deal of difference. Extremes, of course, were bad, but generally speaking the question of acoustics in the studio had little effect on the reception at the receiving end. It had to be remembered that there were many bad sets in existence in the country.

Some speakers at the microphone preferred to hear themselves when they spoke, and others did not. Some even blocked their ears when they spoke, while others had headphones in order that they might be sure of getting their voice coming back to them.

He had been asked a question about crooners. The whole question of crooning was very much in dispute. But crooning, after all, was only possible by the use of the microphone. It was a microphone trick. If the microphone were taken away from the crooner the audience would not hear a word, perhaps not a sound, and, of course, clarity of speech when one was talking or singing very quietly into a microphone was easily possible. It gave the greater opportunity of obtaining the values of the vowels and consonants. If the crooner suddenly opened his lungs and sung at the top of his voice, again, probably, the audience would not be able to hear clearly a single word.

Mr. V. E. Negus said that the first interesting point about the range of voice was that the human capacity for hearing must be attuned to the range of the human voice. Fish, for example, could perceive sounds very much lower than those which were audible to the human ear, because they lived in a different medium. Some animals like shrews and bats no doubt had a range of hearing set to a higher pitch. In an audiogram it was obvious that the range of hearing did exceed the limits of speech. The diagram which the President showed indicated only the fundamental sounds. In the construction of the receiving set and in the hearing aids it was not the fundamental which counted for very much. Hartridge in Starling's "Physiology" showed that one could cut out all the lower pitches, including the fundamental, without diminishing the audibility for speech, and the important range appeared to be between 500 vibrations and 4,000. The overtones which made up the pattern of speech, whereby people guessed the meaning of the words, could be very high, and on a pitch of 2,000, if the overtones extended for three octaves above, the highest overtones were extremely high. The overtones varied in their intensity, the low ones being amplified more than the high, and it was the pattern of overtones which made the speech intelligible.

The male voice, speaking on a lower pitch, had overtones of a lower pitch than the female and therefore was likely to be more easily audible to the person who had lost the high tones.

In the graphs shown by the President the important part of the curves was the range between 500 and 4,000 and one saw on those graphs that in many cases the low tones were retained more or less normally while the high tones from above 500 were largely lost. That would make the speech unintelligible, and if a receiving set could be made which cut out the low tones and amplified the high, it would be a very useful thing for a person who had got this high tone deafness.

On another point the masking effect of low tones was very much greater than the masking effect of high, and if the fundamental of a person's voice were amplified one thereby drowned the overtones. If the fundamental were cut out and one did not have the masking effect of that very loud tone (because the fundamental was always louder than the overtones) then the overtones, which were important, would be better heard. It was also said that one could cut out sounds not only below 500 and above 4,000, but even below 600 and above 3,000, and still retain audibility for speech. That was the simple explanation, he thought, of the reason why the male voice was more audible than the female, and the correction could only be made, in his opinion, not by the person turning on his wireless receiver more loudly, but by some selective mechanism which could reduce these lower tones. This was a subject which must be considered in detail, and he suggested that possibly it might be a good line of discussion, because it was not only of interest but open to possible help for the large number of slightly deaf people to whom reference had been made.

Major E. P. Fowler (U.S. Army) emphasised what Mr. Negus had just said. He thought he was very generous in saying that the most important parts of the pitch were from 500 to 4,000. Tests had shown that the important part was even smaller than that. He would have said the range was from 800 to 2,500 or certainly not over 3,000, and perhaps from 1,000 to 3,000. Certainly 80% of speech intelligibility had that frequency and if one cut out everything below 1,000 and above 3,000 one would get something like 80 per cent. of intelligibility in what was said. One could begin to understand speech at 30% intelligibility.

The characteristics of good speakers had been elicited by actual measurements. They were said to have clear voices or easily understandable voices because they did not drop their voices for certain words. The untrained speaker would let his voice fall off at the end of a sentence; he would not articulate the consonants as well as the trained speaker. The consonants, especially s, t, and th, were the letters on which the intelligibility of speech largely depended. He thought that something should be done about that. If Radio speakers and others were taught to emphasize the consonants then the old people who did not hear above 2,000 would be able to follow the broadcast. If one examined one's patients one would find that over a series of audiometer readings the upper end tended to fall off, but they did not complain of lack of audibility until they dropped off markedly at 2,000. In his opinion the importance of the low tone loss as compared with the high tone loss in otosclerosis had been over-emphasized.

Dr. Douglas Guthrie said that it was obvious from the discussion that the important part of the speech was not loudness, but speed and pitch. Very little had been said about pitch except that, as they all knew, the female voice was not as suitable for broadcasting as the male. But the question of pitch was important. People facing the microphone sometimes became excited and the pitch rose so that they found themselves speaking at a higher level of tone than they would employ in ordinary circumstances.

The pause was even more important. It had been estimated that about 30% of our speech was silent. It consisted partly of pauses, and the point of the pause was of very great importance. The pause before making an important statement or after making it, or, after the fashion of the Prime Minister, during the important statement, added a great deal to its emphasis and to its intelligibility. But it was not simply a matter of words. Mr. Snagge had shown how various speakers had different rates of speaking. The average appeared to be about 160 words per minute. But those words might be long or short. One would have to take a test over a long period if the number of words were to be taken as the criterion. What they should rather do was to gauge the number of speech sounds. A word might contain several speech sounds, and the speech sound or phoneme was the unit, and the phoneme might last from one-thirtieth to about one-tenth of a second. Mr. Snagge had mentioned "Professor Higgins" and although that character was intended by Shaw as a skit, he thought it rather a pity that the B.B.C. had not time to employ a Professor Higgins. The characterization contained a germ of truth, namely.

explanation of the production of fluid in the middle ear after otitic barotrauma. It is probable that the extremes of difference in pressure between that in the middle ear and that in the surrounding atmosphere in otitic barotrauma do not exist in the condition under discussion. Change in pressure, due to closed Eustachian tube, undoubtedly is present, but other factors must also be present, else most Eustachian tube closures would be followed by the presence of fluid in the middle ear. There is some evidence, it seems to us, that there are, in addition, biochemical changes which allow serum to escape from the tissues more readily than usual but lacking proof of these we do not care to do more than mention their possibility.

Pathology

The picture of acute inflammation of the ear with effusion of fluid which does not go on to suppuration is a familiar one. There has not been sufficient stress, however, put upon the fact that the process is one which involves the entire middle ear and not the tympanic cavity alone. When a fluid level line is seen through the drum there is a tendency for the observer to limit his thinking to the part under observation, i.e. the tympanic cavity. The process involves the mastoid cells as well, and this fact accounts for the rapid reappearance of fluid after removal of some from the tympanic cavity by mechanical interference. X-rays of the mastoid will give suggestive evidence that this is so, and operation on this structure does reveal the presence of fluid in the cells. As time elapses, the process passes from an acute to a subacute condition with protracted recovery. Robinson (1942), in studying the biochemical features of the two stages, has shown that the effusion in the acute stage is an exudate. He states that: "It has a high protein content with many polymorphonuclear leucocytes. The effusion in the subacute type is a transudate. There are few polymorphonuclear leucocytes, there is a low protein content, and when the fluid has been present in the middle ear long enough to cause the beginning of the chronic catarrhal stage with its adhesions, large mononuclear leucocytes and epithelial cells make their appearance." Robinson feels that the presence of fluid in the ear is due to a block in the lymphatic glands which drain the middle-ear region. This may be true if it follows the inflammatory conditions which so often precede the presence of fluid in the ear, but it hardly explains the appearance of fluid in cases which are apparently due to allergy, metabolic disturbances or trauma. It is known that if the fluid is unrelieved it gradually loses some of its fluid content. In the later stages of this condition we have all had the experience of removing material from the ear which would string out two or three inches before its rubbery quality would allow it to break and then cause the aural portion to snap back into the ear. Subsequently the fluid can act as a foreign body in the ear. Inflammation, necrosis, ulceration and then infiltration with fibrin follow and in due time organized adhesions take the place of the original matter. It is our feeling that the neglect of this condition is often the precursor of the middle ear with adhesions which is the dread of all otologists. It appears to us that adhesions are as likely to follow this condition as they are to be the aftermath of a suppurative otitis. Certainly additional attacks occur in ears which have already suffered in various degrees from previous secretory otitis, and probably this is because the conditions which created the first occurrence are still present. If we are to be preventers of deafness we must be alive to the possibilities which follow after secretory otitis media. Its neglect, whether purposeful or unintentional, is serious.

Diagnosis

A typical history will usually tell of deafness in one or both ears following a cold. In a fair percentage the story of the cold cannot be elicited. Examination in the inflammatory stage shows dilatation of the blood-vessels of a drum, whose landmarks are still present. Add a conductive hearing loss somewhat out of proportion to the amount of pathology seen and it makes one suspect the presence of fluid. At a slightly later stage the observation of a meniscus makes the diagnosis easy. Occasionally one sees an unusual picture. Two are recalled. One in which there was a frothy top to the serum giving the meniscus the appearance of the "head" of a glass of beer. A second, in which the collection of fluid followed a blow on the head, showed a drum with a red meniscus. Evidently just enough red blood cells had escaped from the vessels to allow them to float to the top of the serum and give this picture. Bubbles of air in the fluid give a characteristic appearance. If there is doubt about the existence of these the use of the pneumatic otoscope is of material aid. A line which does not move with the same rapidity as the moving drum should lead one to suspect the presence of fluid. More difficult to diagnose is the ear, the tympanic cavity of which is completely filled with serum and the only identifying feature is the over-all amber colour of the drum. Often

[*February* 4, 1944]

Some Clinical Observations on Acute Catarrhal Otitis Media

By Major GORDON D. HOOPLE, U.S.A.M.C., and IRL H. BLAISDELL, M.D.

WE intend to limit our remarks to the acute catarrhal otitis medias which are complicated by the presence of non-purulent fluid in the middle ear. These are known by such names as acute catarrhal otitis media with fluid, acute serous otitis media, acute secretory ears, &c. No terminology has been brought to our attention which seems adequately descriptive. In this paper the condition will be referred to as acute secretory otitis media.

We have often been confronted with the following situation. A patient will come to the office and upon examination will have a collection of fluid in one or both ears. The condition will be explained to the patient and then the inevitable question will be asked, "How long will it take to cure me?" In the light of our experience the answer has been, "I do not know". We have been struggling for some years to find a better answer to the question. In medicine the answer, "I do not know", must often be given. For the condition under discussion it may not be necessary to use it any more frequently than in other diseases but it has been our experience to hope, in a particular case, to have the ear free from fluid in a few days, only to find that when this finally happens many weeks have passed. What do we know of the ætiology of fluid in the middle ear? In general it may be said that anything which will contribute to Eustachian tube swelling and closure can be a contributing factor. By far the most frequent of these are the acute inflammatory conditions of the nose and nasopharynx the inflammation from which travels up the Eustachian tube mucosa to the tympanic cavity. The presence of adenoids or large masses of lymphoid tissue in the nasopharynx adds to the likelihood of the onset of secretory otitis media. Lymphoid tissue well up in the Eustachian tube is also an offender. Sinusitis and tonsillitis are members of the inflammatory group which are precursors of this condition. Structural abnormalities of the ears, nose or throat can be contributory. Allergy, metabolic disorders, dental malocclusion, trauma and especially otitic barotrauma are other causative factors. Recently we studied the ætiological factors in 748 patients with acute secretory otitis media which, during the past fifteen years, had been diagnosed as such in our office.

Of these 422 were females and 326 males. This discrepancy between the sexes is without significance. The right ear was involved in 210 patients, the left in 209, while there was fluid in both ears in 329 patients. The average age of this group was 28 years. Search for the causative factor in this group revealed that 619 patients of the 748 had infection of the nose or throat just prior to the onset of ear symptoms, and in 8 cases the ear difficulty arose as a result of some one of the contagious diseases. Maxillary sinusitis on the homolateral side was present in 42 instances. Acute tonsillitis and infection in the adenoid tissue occurred in 47 cases. Acute ethmoiditis was present in 7, and acute sphenoid sinusitis in 1 case. 107 patients showed a marked deviation of the nasal septum to the affected side.

100 patients in the group showed no evidence whatever of infection, either before or during the course of the ear involvement. This group was made up of the following types: Those due to allergy 68; definite endocrine problems: (*a*) hypothyroid 19; (*b*) hypopituitary 2; pregnancy 2; aero-otitis 7 (this does not include closure of the tube nor hæmatoma of the middle ear); trauma 2.

One of us (G. D. H.) during a short Army experience has examined 32 cases. 12 were right sided, 12 were left sided and 8 were bilateral. Almost all of these followed acute upper respiratory infections. Two were due to trauma—blows upon the head. In about a third it was felt that the tonsils and adenoids and particularly the latter were obstructive factors. If the adenoids were present, treatment was of longer duration in each instance. Seven were observed to have an allergic mucous membrane.

As the ætiological evidence given in these two groups is reviewed and that which has long been recognized as predisposing to the accumulation of fluid in the ear is also considered, it emphasizes that any condition which creates swelling in the region of the Eustachian tube can be a causative factor. But this is not the whole story. If it were, every blocked Eustachian tube would be followed by a secretory otitis. But we know this does not always occur. On several occasions we have treated patients with secretory otitis only to have a cold added to the picture just before recovery was about to take place. Occasionally this caused a return to the original condition. More often, despite a closed tube, there was no reaccumulation of fluid. I (G. D. H.) was very much interested, at the last meeting of this Section (December 3, 1943), to hear Squadron Leader McGibbon's

explanation of the production of fluid in the middle ear after otitic barotrauma. It is probable that the extremes of difference in pressure between that in the middle ear and that in the surrounding atmosphere in otitic barotrauma do not exist in the condition under discussion. Change in pressure, due to closed Eustachian tube, undoubtedly is present, but other factors must also be present, else most Eustachian tube closures would be followed by the presence of fluid in the middle ear. There is some evidence, it seems to us, that there are, in addition, biochemical changes which allow serum to escape from the tissues more readily than usual but lacking proof of these we do not care to do more than mention their possibility.

Pathology

The picture of acute inflammation of the ear with effusion of fluid which does not go on to suppuration is a familiar one. There has not been sufficient stress, however, put upon the fact that the process is one which involves the entire middle ear and not the tympanic cavity alone. When a fluid level line is seen through the drum there is a tendency for the observer to limit his thinking to the part under observation, i.e. the tympanic cavity. The process involves the mastoid cells as well, and this fact accounts for the rapid reappearance of fluid after removal of some from the tympanic cavity by mechanical interference. X-rays of the mastoid will give suggestive evidence that this is so, and operation on this structure does reveal the presence of fluid in the cells. As time elapses, the process passes from an acute to a subacute condition with protracted recovery. Robinson (1942), in studying the biochemical features of the two stages, has shown that the effusion in the acute stage is an exudate. He states that: "It has a high protein content with many polymorphonuclear leucocytes. The effusion in the subacute type is a transudate. There are few polymorphonuclear leucocytes, there is a low protein content, and when the fluid has been present in the middle ear long enough to cause the beginning of the chronic catarrhal stage with its adhesions, large mononuclear leucocytes and epithelial cells make their appearance." Robinson feels that the presence of fluid in the ear is due to a block in the lymphatic glands which drain the middle-ear region. This may be true if it follows the inflammatory conditions which so often precede the presence of fluid in the ear, but it hardly explains the appearance of fluid in cases which are apparently due to allergy, metabolic disturbances or trauma. It is known that if the fluid is unrelieved it gradually loses some of its fluid content. In the later stages of this condition we have all had the experience of removing material from the ear which would string out two or three inches before its rubbery quality would allow it to break and then cause the aural portion to snap back into the ear. Subsequently the fluid can act as a foreign body in the ear. Inflammation, necrosis, ulceration and then infiltration with fibrin follow and in due time organized adhesions take the place of the original matter. It is our feeling that the neglect of this condition is often the precursor of the middle ear with adhesions which is the dread of all otologists. It appears to us that adhesions are as likely to follow this condition as they are to be the aftermath of a suppurative otitis. Certainly additional attacks occur in ears which have already suffered in various degrees from previous secretory otitis, and probably this is because the conditions which created the first occurrence are still present. If we are to be preventers of deafness we must be alive to the possibilities which follow after secretory otitis media. Its neglect, whether purposeful or unintentional, is serious.

Diagnosis

A typical history will usually tell of deafness in one or both ears following a cold. In a fair percentage the story of the cold cannot be elicited. Examination in the inflammatory stage shows dilatation of the blood-vessels of a drum, whose landmarks are still present. Add a conductive hearing loss somewhat out of proportion to the amount of pathology seen and it makes one suspect the presence of fluid. At a slightly later stage the observation of a meniscus makes the diagnosis easy. Occasionally one sees an unusual picture. Two are recalled. One in which there was a frothy top to the serum giving the meniscus the appearance of the "head" of a glass of beer. A second, in which the collection of fluid followed a blow on the head, showed a drum with a red meniscus. Evidently just enough red blood cells had escaped from the vessels to allow them to float to the top of the serum and give this picture. Bubbles of air in the fluid give a characteristic appearance. If there is doubt about the existence of these the use of the pneumatic otoscope is of material aid. A line which does not move with the same rapidity as the moving drum should lead one to suspect the presence of fluid. More difficult to diagnose is the ear, the tympanic cavity of which is completely filled with serum and the only identifying feature is the over-all amber colour of the drum. Often

the short process and the handle of the malleus will take on a chalky white appearance in contrast to the amber effect. Alexander has said: "You are not an otologist until you can see amber." These are true words. But still more difficult to diagnose is the ear filled with fluid, the drum of which is so thickened that there is no change in colour. In this instance the diagnosis must be made with the auscultation tube. These are the cases which are most often missed for the loss of hearing present is blamed on the thickened drum. Under these circumstances when auscultation is practised, if there is some air in the tympanic cavity, there is a resulting bubbling which denotes the presence of fluid, but if the tympanum is filled with fluid an entirely different auscultatory effect is heard. It is like the chug of fluid heard in an incompletely filled airtight barrel but even this description is inadequate. It is the most difficult sound in auscultation to recognize and interpret. It is more clearly heard when very gentle inflation is practised. It can easily be missed by a loud blow. For this reason we do not like the use of air-pressured mechanical inflation. The hand-controlled rubber Politzer bag is, we think, diagnostically finer. In all of these stages the drum is usually retracted but this is not universally so and is not a pathognomonic sign.

There is no characteristic hearing curve, for the pathology under discussion may and often does occur in ears already diseased. Pre-existing inner-ear disease may be present also. In an uncomplicated ear, the presence of secretory otitis will, of course, give the picture of a conductive deafness. Usually the deafness is out of proportion to the pathology seen on examining the ear, though on occasion the fluid is in such position that it does not block the conductive pathways and the hearing is quite good.

The importance of stressing the diagnostic features cannot be overdone as they are often overlooked. When students are instructed, it seems that it is necessary to spend more time reviewing the evidence in these cases than in any other of the common ear conditions. Army experience supports these views. Indicative of this is the fact that we have had three cases in our hospital in England, one of which existed five months and two others for six months prior to admission. If the point is overstressed it is because we recognize our own shortcomings and realize that we have had our share of missed diagnoses in this regard.

Interesting as the otological picture may be, diagnostic interest and acumen should not be directed to the ear alone. It has already been mentioned that 100 patients of our civilian series did not show any evidence of infection either before or during the course of the ear involvement. Of these, 68 were obviously allergic. A majority of them had their ear complication during the hay fever season when the nose was blocked. The endocrine cases, numbering 21, were fairly obvious. Most of these were referred back to their own physicians for complete check-up including basal metabolic rates. As a result, 19 received thyroid in appropriate dosage, even as high as six grains per day. In all these cases the ear situation improved shortly afterward. The two cases recorded as hypopituitary problems were referred back to one of the local obstetricians, for both of these were women who had been under his care for delivery some months earlier. It was at his suggestion that anterior pituitary lobe hormone was used in both instances, and apparently with excellent results, for the ear condition rapidly improved after having been static for several weeks. Of the two patients who developed acute secretory otitis media during pregnancy, both showed symptoms during the last trimester of pregnancy when the nose was particularly engorged. Both cleared up completely shortly after delivery. It is interesting to note that one of these patients subsequently became pregnant and again showed the typical picture with fluid in both ears.

The cases of otitic barotrauma need no special mention, except that they occurred as a direct result of flying, and apparently without evident infection of the nose or throat.

Here then is a breakdown of 100 patients who had ætiological factors other than acute infections of the nose and throat. It suggests that some of these factors may be present in the patients who do have acute infections and the failure of their discovery leads to a protracted course of treatment. And it further suggests that there may be ætiological factors which we have not yet unearthed, the discovery and correction of which may lessen the likelihood of a lengthy illness.

Prognosis

Under the heading of Pathology, mention has been made of two types of secretory otitis media, i.e. the acute and the subacute. The majority are acute and recover in a relatively short period. A continuation of causative factors is undoubtedly a major item in the translation of an acute condition into a subacute affair. Without any evidence to support the view, we have the feeling that there is the occasional case which has the subacute features from the start. At least these cases will persist for some time despite the best therapy one can apply. This suggests also that some

underlying factors have not been discovered. The borderline between the acute and subacute is not sharp and it is with difficulty that one can say which patient belongs to the former group and which to the latter. Certain it is that the subacute cases are the difficult ones to clear. Just when these should be further classified as chronic is also difficult to state though it would seem they should be classified as subacute as long as the transudate is still fluid. When, and if, this is replaced by adhesive processes the chronic stage may be said to have begun.

If the condition can be cleared the hearing in almost every instance returns to its former level. Unless subsequent attacks produce adverse conditions the ear apparently is as good functionally as before. On the other hand if the pathological state persists, eventually changes take place which are detrimental to function and these are irreparable.

In the civilian series above mentioned the average number of treatments per patient was six. This figure does not give the true picture of the average length of time of treatment for many were treated only once or twice and then did not return. Others were treated numerous times over a period of months and still were not entirely free from symptoms. Of the total of 748 there were 15 who were definitely not improved after considerable treatment. There was one patient in whose ear there was persistence of fluid for six months and another, with bilateral involvement, had fluid in the ears at the end of a year despite all the forms of treatment which were tried.

In the military series, where control of the patient is much more satisfactory from two standpoints, namely (1) compulsory return visits and (2) management (rest, diet, &c.), results were more satisfactory. None of the patients failed to recover and each testified that hearing had returned to its former level. The shortest period between the institution of treatment and recovery was two days, the longest was sixty-three days, while the average was just under twenty-two days. There was a notable agreement between the length of time symptoms had persisted prior to treatment and the period required for recovery. If treatment was instituted shortly after onset there was a short convalescence. Neglect before treatment almost universally was followed by a protracted recovery.

In both series the presence of complicating factors seemed to be correlated to retarded response to treatment. It is quite probable that undiagnosed complications were the cause of some of the disappointing responses.

Treatment

These patients were seen over a span of seventeen years and as might be suspected the management of them was not the same during the whole of this period. In the later years, however, a fairly definite pattern was followed. An attempt was made, when a patient asked for consultation, to determine the ætiological factors present. Patients were classified, if possible, into two groups, (1) those of infectious origin and (2) those of non-infectious origin. Elimination of the infection was the first goal of the treatment of the patients with acute inflammation. Quite often patients were classified as belonging to this group on the history only, for by the time they had presented themselves for treatment of the ear the initial infection had subsided. In either event, for patients in this group, nothing was done to the ear until the infection had cleared. Following this, catheterization with gentle inflation was done if the collection of serum had persisted. If one or two catheterizations did not result in a diminution of the symptoms, paracentesis of the membrana tympani was done and the ear was inflated to allow the escape of some of the fluid. Occasionally gentle suction was used to assist in its removal. Subsequent paracenteses were done at two, three, four or five day intervals if there was a persistence of the fluid. Paracenteses were repeated at such intervals until the condition had cleared. Patients in the second or non-infectious group were first cultured for evidence of infection in the nose and nasopharynx. If these were negative, search was then made for other causative factors.

If an allergy survey did not yield satisfactory results, the endocrine difficulties were considered. Since some allergic individuals have a consistently low basal metabolic rate, it did not seem advisable to order such a test on all patients of this group, lest we classified them as hypothyroids. The basal metabolism plus a sugar tolerance test differentiated those having a low rate due to allergy and those who really were hypothyroids. When the war broke out we were carrying on a study of the microscopical comparison of the middle-ear mucosa in the normal and in thyroidectomized guinea-pigs and in pigs which had been sensitized to various allergens. We hope at some later date to finish this work.

In the so-called subacute or protracted cases such additional therapy as seemed

indicated was instituted. Thus, some were put on allergic management, some had surgical removal of lymphoid tissue from the nasopharynx, some had X-ray therapy to this locality, and others were placed on insulin, thyroid substance or other appropriate medication. We did not use radium therapy in the nasopharynx, though there is growing evidence this may prove a valuable adjunct in the treatment of this condition.

Comment

It has been taught in the past that catheterization in this condition only adds to the œdema present in the tubal mucosa and prolongs the condition. For this reason, politzerization has been advocated. But, with us, politzerization in the latter part of the civilian series was discarded for two reasons, one diagnostic and the other therapeutic. Diagnosis of fluid in the ear by inflation (which is often necessary) cannot successfully be made in all cases unless a very gentle inflation is done. There are too many accessory noises in the usual politzerization. Therapeutically it has been discarded because repeated politzerizations failed to bring about the desired results in a reasonable time. Catheterization without paracentesis failed in like manner to bring about an early cure. Exactly why these two methods were apparently ineffective we cannot say. Their purpose is to open the Eustachian tube and its opening should be followed by some escape of fluid through it into the nasopharynx. But this does not always happen. In fact, far too frequently it does not. We are confident that many patients in these two series had patent Eustachian tubes long before the fluid disappeared. At least in many of them, in the later stages, most gentle catheterization would cause air to pass unimpeded into the tympanic cavity (an open Eustachian tube) though fluid was still present, perhaps in large quantity. The conclusion has been reached, therefore, that the blowing of air into the intact middle ear is not an efficient method of treatment for this condition.

Shahinian (1943) postulates that catheterization in this condition performs two functions. One blow dilates the tube and the tympanic cavity (by means of the membranal bulge) and subsequent blows force fluid from these dilated spaces out around the catheter's end into the nasopharynx. He maintains that there is often insufficient dilatation of the tympanic space because of the character of the fluid or beginning adhesions. He proposes a controlled and measured suction in the external auditory meatus which will cause a bulge of the drum and suggests that, relieved of the necessity of the tympanic dilatation, the efficiency of the catheterization will be increased. This method has not been tried in any of the cases under discussion.

Paracentesis without anæsthesia has been carried out in 422 patients. Puncture, not incision, is made in the membrana tympani at 6 o'clock just central to the annulus. Subsequent catheterization, if the accumulation of fluid has been great enough to warrant it, affords considerable relief and marked improvement in the hearing. There have been no unfortunate sequelæ to this manipulation, though it has been repeated many times in the same patient. One ear did go on to suppuration while paracentesis was being used but the onset of this complication was concomitant with the start of a cold. This ear was dry and hearing had returned to normal within a fortnight. The spacing of the paracenteses at two, three, four or five day intervals depends on the otological picture and the patient's symptoms.

It is not the purpose of this paper to advocate paracentesis for this condition, as there were no series of controls and consequently comparison with other procedures is pointless, but it has been a useful procedure in the series presented. While the escape of some fluid from the tympanic cavity does not alter very much that which still lies in the mastoid cells, it does afford, apparently without future harm to the ear, a marked relief in symptoms.

Fifteen cases were definitely not improved after considerable treatment with the methods just outlined. Cody (1941) and Robinson have both recommended mastoidectomy in the protracted subacute cases. One wonders if some of the fifteen just mentioned might not have been cleared by such a procedure.

REFERENCES

CODY, CLAUDE C., Jr. (1941) *Tex. St. J. Med.*, 37, 233.
ROBINSON, J. MATHEWS (1942) *Sth. med. J.*, 35, 815.
SHAHINIAN, LEE (1943) *Arch. Otol. N.Y.*, 38, 328.

Section of Orthopædics

President—S. Alan S. Malkin, F.R.C.S.Ed.

[*January* 4, 1944]

The Relative Importance of Periosteum and Endosteum in Bone Healing and the Relationship of Vitamin C to Their Activities

By Geoffrey H. Bourne, D.Sc.

Mackenzie Mackinnon Research Fellow of the Royal College of Physicians of
London and the Royal College of Surgeons of England

(*From the University Laboratory of Physiology, Oxford*)

Introduction

Since the time of John Hunter (1835) there have been a multiplicity of hypotheses as to the relative functions of the various units of bone structure in bone regeneration which include that of Cohn and Mann (1915) who claimed that the bone cells themselves (the osteocytes) were responsible for regeneration. Leriche and Policard (1928) mainly as a result of speculation attributed the whole of the function of bone regeneration in fracture healing to the formation of bone from the connective tissue of the callus, Keith (1928), Girdlestone (1932), and Harris (1933) have stressed the importance of the osteoblast in bone formation. Hertz (1936) has noted that multiplication of cells and hyperæmia followed by the formation of bony trabeculæ occurred between the fibrous layer of the periosteum and the surface of the bone, after injury; but he noted that this reaction was greatest some distance from the fracture and that it diminished the closer the line of fracture was approached. This reaction he described as the "distant periosteal reaction". He found a multiplication of cells and hyperæmia close to the fracture line in the endosteum, but there was no "distant endosteal reaction". Some of the callus then ossified directly and the remainder became cartilaginous and subsequently underwent endochondral ossification. Urist and McLean (1941) have made the following rather interesting statement concerning the healing of a fracture: "Our preparations demonstrate invasion of the fibro-cartilaginous callus by new bone, which calcifies as it advances into the callus mass, and affords striking evidence that the bone originates outside of this mass. This process is analogous to the intra-cartilaginous growth of bone, in that the remnants of the invaded tissue are made use of and converted into bone matrix by the invading osteogenetic cells. . . . According to our observations, new intra-membranous bone is formed, chiefly from the deep or cambial layer of the periosteum and from the endosteum, including the osteogenetic cells within the Haversian canals."

Experimental

The stimulus to repair after a fracture is very great and rapid and since it is impossible to obtain a series of identical fractures (although the 1936 technique of Hertz approaches this ideal fairly closely) it is impossible by killing fractured animals at different times and examining sections of the fracture to be sure that one is observing the correct sequence of events in healing—since the process will proceed at different rates in different types of fracture. For the purposes of this work, therefore, small 1 mm. holes have been bored (with the aid of dentist's twist drill, using an aseptic technique; *see* Bourne, 1942*a*, for details) in the femora and in the parietal region of the skull of guinea-pigs and rats. By this means it is possible to obtain a small standardized area of regeneration and by

killing animals at different intervals one can be reasonably sure of obtaining a continuous sequence of stages in the healing process.

Very little difference has been found in the healing processes in holes bored in the femora of rats and guinea-pigs. The process of healing is also fundamentally the same in the healing of holes in both the skull and the femora of guinea-pigs although it is slower in the former and in the latter small amounts of cartilage are sometimes formed.

Hertz (1936) found that in the healing of fractures of the fibula in rat and guinea-pig there were two processes of ossification: (1) Direct and (2) Endochondral. In the rat he found the second process to play a more important part than the first. Since in the repair of the holes described in this paper, there is little cartilage found in any case, this difference in healing between the two species was therefore eliminated; the one description will serve to show the healing processes in both. Animals were killed at twenty-four hours, three days, five days, one week and two weeks after boring the holes. The bone bearing the hole was removed at autopsy and fixed, in some cases in 5% formol saline and in others in acetic acid silver nitrate. The object of the latter fixative was to demonstrate vitamin C histologically in bone repair, but there were so many factors complicating the reaction in healing bone that it was not possible to obtain reliable results. After fixation for twenty-four hours, the bones were decalcified for a further twenty-four hours in trichloracetic acid. They were then washed, dehydrated, embedded in wax, sectioned, stained with hæmatoxylin and van Gieson and mounted in balsam.

In the specimens used for the section on the relation of vitamin C to the periosteum and endosteum, groups of animals were placed on a scorbutic diet (the same as that described by Bourne, 1942b) for two weeks and various animals were given different doses of vitamin C.

No. of Animals						Amount of Vitamin C
5	...	...	...	...	...	2 mg.
5	...	...	...	...	...	1 mg.
5	...	...	...	...	...	0·25 mg.
5	...	...	...	...	...	no supplement given

At the end of the first week a hole was bored in each femur of each animal. At the end of the second week, all animals were killed and their femora treated as described above.

Immediately the hole was bored there was a hæmorrhage from the medulla. The blood soon clotted and within twenty-four hours of the operation the clot became invaded by cells which had the appearance of fibroblasts and which were probably osteoblasts. They appeared to come from the periosteum and the marrow. By twenty-four hours signs of fibrous organization were apparent. The cells gave the appearance of having moved through the clot spinning fibres as they went. Danielli (1942) has pointed out that strands of protein can be spun from the surface of protein monolayers which have the same molecular orientation as collagen fibres and he suggests that these fibroblasts "spin" such fibres from a layer of protein absorbed on their cell membranes. These first fibres which were produced in the clot were very fine, and since they did not retain van Gieson stain (which gives a bright red colour with mature collagen) they were probably in the nature of reticular "pre-collagen" (Hunt, 1941) fibres. This process of fibre production continued for the next two days. By this time (three days after the operation) most of the blood corpuscles of the clot had been removed and their place taken by a close network of mixed collagen and "pre-collagen" fibres. In the case of holes bored in the guinea-pig's skull, however, there was often a considerable amount of the original blood clot still present at the end of a week. In such cases, the clot had frequently caused the formation of a deep depression in the brain substance.

By three days after the operation a marked reaction could be seen in the cambial (inner cellular) layer of the periosteum. The cells in this region had proliferated and lifted the fibrous layer of the periosteum away from the bone. This process spread outwards from the hole for some distance (a centimetre or more). By the end of three days the fibrous layer of the periosteum appeared to be growing over the fibrous callus which had formed. The periosteal fibres engaged in this migratory activity behaved like true collagen because they retained van Gieson stain. Small splinters of bone which were present in the hole in some cases as a result of the boring were in the process of being broken down and reabsorbed. Those which had a small piece of periosteum attached to them, however, showed activity of the periosteum. At three days bony trabeculæ appeared to be forming in the region of the endosteum and apparently in

association with it. This process appeared to take place by the progressive metamorphosis of the adjacent pre-collagen fibres and their arrangement into thick trabecular strands. The first formed trabeculæ were always associated with the endosteum and some endosteal trabeculæ were always present before bone was formed by the periosteum.

At four days a striking feature of the healing process was the formation of numerous osteoid trabeculæ (which stain intensely with van Gieson after decalcification) in the proliferated cambial layer of the periosteum. In some cases, by this time, the reaction had travelled completely round the femur. In some specimens the fibrous layer of the periosteum had by this time penetrated into the callus from the periosteum. It seems that the behaviour of the periosteum is one of the factors which influence the rate and orderliness of the healing of bone. The main function of the fibrous layer of the periosteum appeared to be to grow across and seal off the repair tissue from the tissues outside the bone.
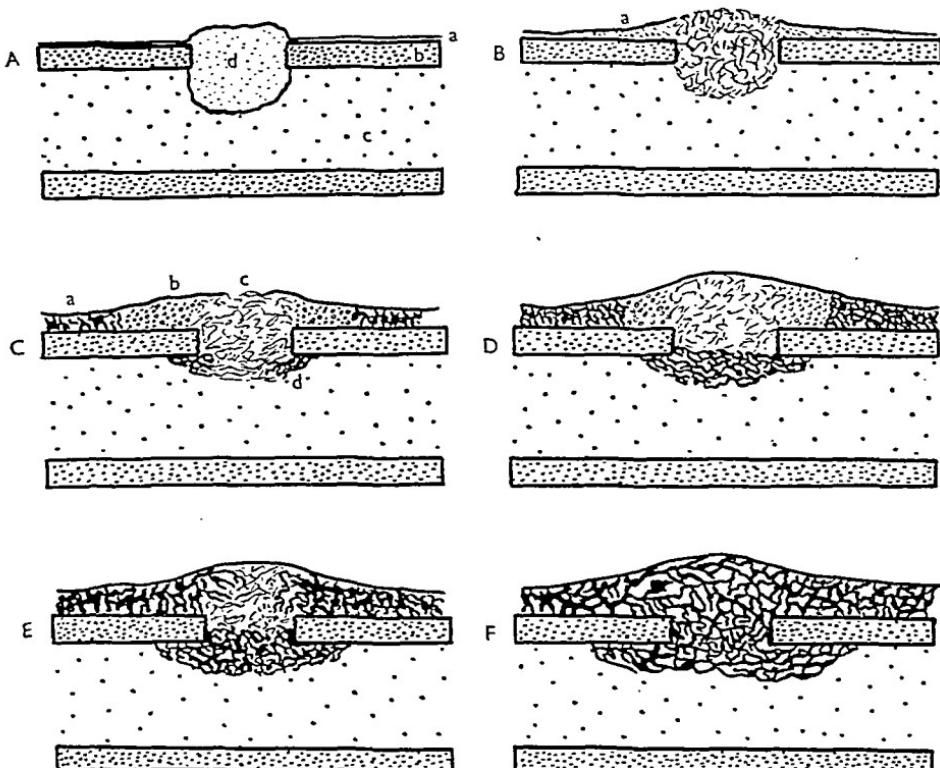
Schematic diagram of healing in a 1 mm. hole bored in a femur of a guinea-pig. A, immediately after injury; B, twenty-four hours after injury; C, three days after injury; D, five days after injury; E, one week after injury; F, two weeks after injury; a, periosteum; b, cortex of femur; c, marrow; d, blood blot. Cellular multiplication of the cambial layer of the periosteum, between the fibrous layer of the periosteum and the bone can be seen in B and C. Periosteal and endothelial trabeculæ can be seen developing in C, D, E and F.

A tendency which the fibrous layer sometimes exhibited to dive into the callus would appear abnormal. In some specimens, where it had not penetrated into the callus it had actually grown completely across the hole by four days.

Some specimens at four days showed the presence of masses of what appeared to be collagenous material apparently derived from the periosteum, which were losing their ability to stain with van Gieson and which appeared to be forming hyaline ground substance. The enclosed cells were altering their appearance and the whole mass of tissue was apparently in an early stage in the formation of cartilage.

By seven days, in every specimen, collagenous strands from the periosteum had passed completely across the fibrous mass plugging the hole. In some cases, on either side

of the hole some of the periosteal trabeculæ had a cartilaginous appearance. The hole was filled in most specimens (with the exception of the holes in the skull) with solid-looking trabeculæ which anastomosed with each other in typical fashion. In other words, the hole was now plugged with membrane bone which acted as a very serviceable repair tissue. In some rat femora, for no obvious reason, the whole medulla became filled with trabeculæ. The maximum number of trabeculæ in the rat appeared to be formed by seven days, but in the guinea-pig it took longer for this to happen (ten to fourteen days). In many skull holes in guinea-pigs there was only a small number of trabeculæ present, even at fourteen days. The bones of the skull, therefore, do not seem able to repair damage as rapidly as those of the limbs.

In the rat by eleven days there were some signs of the formation of cartilage from the osteoid trabeculæ. By the end of two weeks there was a certain amount of cartilage derived from the periosteum and some appeared to have formed from the trabeculæ. There was a thick coat of collagen fibres which was derived from the periosteum. There was no evidence in the guinea-pig that there was a metamorphosis of any osteoid trabeculæ into cartilage.

Relation of Vitamin C to Periosteal and Endosteal Activity

It has been shown by Bourne (1942*b*) that in guinea-pigs receiving less than 2 mg. of vitamin C a day there is a deficient production of trabeculæ in the hole. Since the production of trabeculæ appears to be initiated by the endosteum, this suggests that the endosteal activity can only take place if adequate vitamin C is provided in the diet.

The endosteum is normally composed of a layer of osteogenetic cells closely pressed against the inside of the bone. Also there are endosteal cells lining the Haversian canals. Embryologically they are derived from the cambial layer of the periosteum. When a bone is injured, as for example in the boring of holes described in this paper, there is an enlargement, multiplication and migration of the cells near the injury. The migrating cells appear to form collagen fibres and these are eventually aggregated together into osteoid trabeculæ. In animals receiving no vitamin C there is still some enlargement and multiplication of endosteal cells near the injury and in some cases some fibres are formed. More rarely just the beginnings of osteoid trabeculæ are apparent. Normally the endosteal cells which are situated some distance from the injury, are closely pressed against the bone and are difficult to see. In completely scorbutic animals these endosteal cells are much more apparent. They appear swollen (particularly the nuclei) and in most cases have a pale-staining œdematous appearance. In animals receiving an amount of vitamin C in excess of 0·25 mg. a day, this œdematous condition of the endosteal cells does not appear to be present.

A definite relationship can be observed between the periosteal activity and the amount of vitamin C. (Some particulars of this have been given by Bourne, 1942*b*.)

In an animal receiving no vitamin C there is often, at the end of a week after injury to the bone, no trace of a reaction by the cambial layer of the periosteum. In some cases the cells of this layer undergo a few divisions so that there is a slight thickening, but all other processes are inhibited. The outer fibrous layer of the periosteum does not grow over the tissue filling the hole in the bone in the usual way and the attachment of this layer to the bone is loosened. As a result, it often comes away during the process of sectioning.

In animals receiving 0·25 mg. of vitamin C per day, there is at the end of one week a multiplication of the cambial layer of the periosteum but no formation of collagen fibres by the cells. There is still no sign of the growth of the fibrous layer of the periosteum over the hole in the bone.

In animals receiving 1 mg. of vitamin C per day, the cells of the cambial layer of the periosteum have after a week multiplied to such an extent that this layer is six times as wide as it was in the preceding group. In addition, there are the beginnings of trabeculæ formation. There is some growth of the fibrous tissue of the periosteum over the hole.

In animals receiving 2 mg. of vitamin C the cambial layer of the periosteum at the end of a week has formed solid bony trabeculæ continuous with the bone of the femora and the fibrous layer of the periosteum has grown, in most cases, across the hole, which by now contains an appreciable number of bony trabeculæ.

SUMMARY

This work suggests that both endosteum and periosteum play an important part in the regeneration of an injured bone and that the first reaction and production of repair

bone in the region of the injury is by the endosteum. Only some days after the original sealing off of the injury (in this work, a hole bored through the bone) by the endosteum does the periosteum cover the injured area with a layer of bone. Any cartilage present appears to be formed in the first instance in association with the periosteum, but some cartilage appears to be formed by conversion of osteoid trabeculæ. The activity of both periosteum and endosteum is impaired by a deficiency of vitamin C.

.   REFERENCES

BOURNE, G. H. 1942a) *Quart. J. exp. Physiol.*, 31, 319.
——— (1942b) *J. Physiol.*, 101, 327.
COHN, I., and MANN, G. (1915) *Surg. Gynec. Obstet.*, 20, 661.
DANIELLI, J. F. (1942) *in* Cytology and Cell Physiology, edited by G. Bourne, Oxford.
GIRDLESTONE, G. R. (1932) *Proc. R. Soc. Med.*, 26, 55.
HARRIS, H. A. (1933) Bone Growth in Health and Disease. Oxford.
HERTZ, J. (1936) Studies on the Healing of Fractures. Oxford.
HUNT, A. H. (1941) *Brit. J. Surg.*, 28, 436.
HUNTER, J. (1835) Works. Palmer's edition.
KEITH, A. (1928) *Proc. R. Soc. Med.*, 21, 302.
LERICHE, R., and POLICARD, A. (1928) The Normal and Pathological Physiology of Bone. London.
URIST, M. R., and McLEAN, F. C. (1941) *J. Bone Jt. Surg.*, 23, 1.

Ossifying Chondroma Replacing the Infrapatellar Pad of Fat

By PAUL BERNARD ROTH, F.R.C.S.

THIS condition appears to be one of extreme rarity. I have only been able to find two published cases, one by Cassou in 1936, and one by Robillard in 1941. Cassou's case occurred in the left knee of a man aged 43: no operation was done, Cassou contenting himself with remarking that the ossification caused the owner but little discomfort. Robillard's case concerned the left knee of a woman aged 35, who was admitted to hospital on June 6, 1939.

"Two years before she had injured her knee in a fall. The knee was not X-rayed at the time. The patient had since complained of pain in the knee, and was treated for osteo-arthritis. In March 1939 she fell again, and pain, tenderness, swelling, and immobility of the left knee resulted, persisting until the date of her admission to hospital. Examination revealed a swelling of the left knee, reaching a maximum between the patella and the tubercle of the tibia, with diffuse tenderness and marked restriction of motion. X-rays revealed a large calcified mass, apparently in the anterior chamber of the knee-joint. A utility incision was employed and the patella displaced laterally. The joint cavity was opened and explored. The mass was exposed, dissected free, and excised. It measured 5½ by 4 by 2 cm. . . . The post-operative course was uneventful. Motion at the knee-joint improved until 60 degrees of flexion were present, and the patient was free of pain.

Robillard's case is illustrated, by lateral radiographs before and after operation, by a photograph of the osseous mass, and also by a photomicrograph showing bone trabeculæ.

My case was as follows:

H. P. S., a busy solicitor, aged 69, was sent to me by Dr. Barnet Stross on January 7, 1943, with the history that for twenty years he had had increasing stiffness in the right knee. For the last three or four years he had noticed an enlargement in front. The knee was gradually beginning to ache more and more, especially when near a fire, and he could only go downstairs a step at a time.

On examination.—The knee was seen to be markedly enlarged in front, below the patella: there was a prominence which gave the appearance of a second patella below the normal one. This was of bony hardness, and could be moved by me slightly to either side, but not up or down. The knee could only bend to 90 degrees, and extend to 150 degrees; the movement was accompanied by gross creaking. Any attempt to force the knee beyond these limits at once caused pain and was objected to. X-ray (fig. 1) showed that practically the whole of the space normally occupied by the infrapatellar pad of fat was filled with a dense opaque mass, which gave a much darker shadow than the adjacent bones. I diagnosed calcification of the pad, and advised its removal.

On June 12, under spinal anæsthesia administered by Miss E. M. P. Law, M.B., I split the ligamentum patellæ and patella, exposing the mass, which had the appearance of a large mulberry, being deep purplish red in colour. It was freed easily above and on either side, by blunt dissection with a periosteal detacher; below, a few light touches with a scalpel were needed to free it from the front of the tibia. The two halves of the patella and its ligament were then brought together and secured in position with a continuous catgut suture passed through the overlying fibres of the quadriceps tendon. The skin was closed with Michel's clips.

An X-ray taken on June 18 (fig. 2) showed that the whole of the calcified mass had been removed, with the exception of a very small piece lying just above the tubercle of the tibia.

FIG. 1   FIG. 2

The patient made an uninterrupted recovery, the wound healing by first intention, and left hospital after three weeks, walking with his knee slightly stiff, supported by a wide crepe bandage.

When seen at my house on July 9, to which he had driven himself in his own car, he could bend his knee to 100 degrees: and when seen for the last time on August 27, he could bend his knee to 45 degrees, and extend it fully, and walk up and downstairs in a normal manner without the slightest hesitation. There was nó creaking on movement. He expressed himself as very pleased with the result.

Pathological report.—The specimen weighs 50 g. and measures approximately 5·5 by 4·0 by 2·4 cm.

It consists almost entirely of bone, which at the centre is very hard and compact, but at the periphery is spongy. There are no cysts and no evidence of degenerative changes. The entire mass is covered by a thin layer of cartilage (1 mm.).

The surface is coarsely irregular with several cartilage-covered excrescences, and two facets can be made out which presumably were in apposition with the patella and tibia, respectively. A good deal of connective tissue, in places suggesting synovial fringe, is attached to the surface.

Histology.—There is an outer layer of fairly cellular hyaline cartilage, and deep to this are bony trabeculæ. Ossification is proceeding in the cartilage, but there is no great osteoblastic proliferation, a few osteoblasts are present. Some of the bony trabeculæ are quite dense.

A few hæmopoietic cells are seen between the trabeculæ.

This is most probably an ossifying synovial chondroma.

Comment.—The calcified mass was probably not formed bv ossification occurring in the infrapatellar pad of fat, but was in reality, as Dr. McCall suggests, an ossifying chondroma taking its place. In the course of years as it grew larger, it compressed the soft pad of fat into a smaller and smaller space, causing it to atrophy until it was almost non-existent.

When I removed it an empty space was left which a few days later was found distended whether with blood or synovial fluid, or both, I was not able to ascertain, but I have little doubt that the sub-patella pad of fat has by this time reformed and now occupies its normal position.

I am indebted to Dr. Cyril Bellamy for the X-ray pictures of this case, and to Dr. A. J. McCall for his pathological report upon the specimen removed.

REFERENCES

CASSOU, R. (1936) Calcification de la bourse prétibiale, *Bull. Soc. Radiol. méd. Paris*, 24, 383.
ROBILLARD, GREGORY L. (1941) Ossification of Infrapatellar Bursæ and Fat Pad, *Amer. J. Surg.*, 51, 442.

Posterior Dislocations of the Hip Associated with Fracture

By Major GEORGE HAMMOND, U.S.A.M.C.

POSTERIOR dislocations of the hip do not occur frequently and their association with fracture of the pelvis or head of femur is less common. The frequency of this injury has, apparently, been increasing in recent years due to the increase in severe automobile accidents.

Dislocation of the hip posteriorly is often the result of considerable trauma being applied to the anterior aspect of the knee in the direction of the long axis of the femur when the hip and knee joints are in a position of 90 degrees flexion. As a result of such a force the head of the femur is forced posteriorly and one of three injuries may be caused: (1) posterior dislocation without fracture; (2) posterior dislocation with fracture of the posterior wall of acetabulum; (3) posterior dislocation with fracture of the head of the femur. A posterior dislocation with both of these fractures is very rare.

The posterior wall of the acetabulum may be comminuted but more commonly it is fractured off as a single piece which displaces posteriorly and superiorly with the head of the femur. By manipulative reduction of the dislocation it is hoped that the posterior acetabular fragment or fragments will be well reduced and will heal to form a bony buttress preventing re-dislocation. Unfortunately the fragment or fragments often remain in a displaced position after reduction of the dislocation and this is, not uncommonly, an indication for open reduction, particularly in the case of a large, single fragment. If the head of the femur is involved, it is usually the inferior or antero-inferior one-third that is fractured in posterior dislocations of the hip. The head fragment may remain in the acetabulum where it may or may not be attached to the ligamentum teres, or the fragment may displace out of the acetabulum where it is usually in poor relationship with the intact portion of the femoral head. By closed reduction of the dislocation the fragment may be reduced in very good position. Open reduction of the fragment is the treatment of choice in certain cases in which anatomical reposition is not obtained.

Fracture dislocations of the hip are often associated with severe complications. Too often avascular necrosis of the femoral head or traumatic arthritis or both occur and a poor result is obtained. For this reason a definite prognosis should not be given until at least five years have elapsed from the time of injury. The sciatic nerve may be seriously involved with resultant paralysis of varying degree.

[Eight cases of fracture-dislocations of the hip were presented with the aid of lantern slides and the difficulties of treatment and the early results were discussed.]

As in all intra-articular fractures, anatomical reduction of the fragments should be obtained, if possible, so that the frequency of traumatic arthritis is reduced to a minimum.

Operative reduction is indicated when the dislocation is irreducible by conservative methods; when a large acetabular fragment does not reduce very well as the hip is reduced; when a fragment of the acetabular wall displaces into the acetabulum; and when, in fractures of the head, the fragment is not reduced anatomically. Dislocations complicated by fractures of the shaft of the femur often necessitate open reduction.

The complication of avascular necrosis of the femoral head remains an unsolved problem. Early gentle reduction of the fracture-dislocation and adequate immobilization of the hip during the stage of revascularization may reduce the incidence of this complication. In case of open reduction the operator should be ever mindful of this complication and should strive to minimize further destruction of vessels supplying the femoral head and bone fragments. If necrosis develops it is probably best to delay weight-bearing until the dead bone has been replaced by living bone. Otherwise the weakened necrotic bone may be crushed by the body-weight with marked deformity of the femoral head resulting. Even if there is freedom from weight-bearing degenerative arthritis develops in a large percentage of cases because of the imperfect regeneration of fibro-cartilage covering the head.

In cases complicated by traumatic arthritis or by avascular necrosis with degenerative arthritis and in the late, unreduced cases, vitallium cup arthroplasty as described by Smith-Petersen offers a good chance for a favourable result.

The Hypermobile Ankle

By Major J. Grant Bonnin, R.A.M.C.

In the routine examination of the foot the degree of inversion (tibial flexion) of the hind-foot is frequently observed as a guide to the general flexibility of the foot. The movement is a complex one, consisting of movement at the subtaloid joint and movement at the midtarsal joint; usually combined with some plantar flexion at the ankle. In the normal ankle only plantar flexion is allowed, but in the hypermobile ankle a varying degree of tibial flexion at the ankle-joint occurs. This varies from a barely perceptible twist to a 25 degrees tilt. A tilt of greater degree we have only seen in association with rupture of the fibular-collateral ligament in acute injuries. This condition of hypermobility may be symptomless in the young or in people with developed muscular control, but in a great many people it presents itself as a complaint of "weak ankle". "going over on the ankle", or recurrent sprains. The unilateral hypermobile ankle forms a high percentage (24%) of all sprained ankles examined. Its occurrence on the injured side is the criterion of the severity of the sprain. Hypermobile hind-feet are present bilaterally in patients with severely sprained ankles in a higher percentage (42%) than in a group of normal people (13%).

The hypermobile ankle is a distinct entity capable of radiological proof. Between it and the stiff immobile ankle a gradation of mobility exists. It is possible to show a convincing increase in the number of sprained ankles among those with unusually mobile ankles, and a marked absence of sprains among those with immobile ankles. It is noteworthy that the hypermobile ankle is only hyperinvertible. No cases of relaxation of the deltoid ligament with increased eversion are encountered, except as a result of acute injury. This is due in part to the supporting action of the fibula and in part to the strength of the deltoid ligament, which when it ruptures does so at its periosteal attachment to the medial malleolus, and after adequate immobilization (five weeks) reunites with no relaxation. In contrast to this the fibular-collateral ligament may have either of its two lateral bands torn, the posterior talo-fibular ligament usually remaining intact. In the hypermobile ankle relaxation of the calcaneo-fibular ligament is the most important single causative factor.

The clinical features.—On grasping the fore-foot and endeavouring to invert the whole foot a variable degree of resistance will be met. The opposition met with in spastic flat-foot is well recognized. The lack of opposition which allows the sole to turn at right angles to the transverse axis of the ankle, is characteristic of the hypermobile joint. The normal hind-foot allows medial (tibial) flexion of the calcaneus at the subtaloid joint, so that the lateral aspect of the calcaneus forms an angle of about 20 degrees with the outer margin of the fibula. In the stiff ankle it may deviate only 5 to 10 degrees, while in the hypermobile ankle the outline of the outer margin of leg and foot, seen in profile, resembles the curve of a hockey stick, and the outer surface of the calcaneus may be at 45 degrees to the line of the leg. This degree of mobility is not derived entirely from the subtaloid joint but from added mobility at the ankle-joint.

Normally the prominence of the anterolateral margin of the upper articular surface of the talus can be palpated in front of the fibular malleolus. The ease with which this can be done varies with the amount of subcutaneous fat but as the foot is inverted (and slightly plantar flexed) this margin becomes more prominent. In the hypermobile foot it becomes excessively prominent and the outline of the outer side of the ankle shows three prominences—the external malleolus, the cuboid, and the anterolateral edge of the talus—in contrast to the usual two. It is characteristic of the hypermobile ankle that the prominence of the talus is not only palpable but visible to an abnormal degree.

Inversion is made up of two components, the tibial flexion of the hind-foot at the subtaloid joint, and the adduction and plantar flexion of the fore-foot at the midtarsal joint. These two movements in any foot are not necessarily equally free. It is not uncommon to find marked laxity at the midtarsal joint and a limited mobility at the sub-taloid joint. When this is so, inversion frequently produces great prominence of the head of the talus making a third swelling palpable in front of the fibula. If to this is added marked tibial flexion of the hind-foot, four prominences may be seen— fibular malleolus, anterolateral edge of talus, lateral aspect of head of talus, and the cuboid.

Radiography.—If the normal ankle is examined under inversion strain, even when the

patient is relaxed by a general anæsthetic, the congruity of the upper articular surface of the talus and of the lower articular surface of the tibia remains. In the hypermobile ankle, however, it will be found that the two surfaces subtend an angle which varies from 3 degrees to 25 degrees, and that this range of movement is proportional to the degree of hyperinversion possible. The condition may be present on both sides and when so both subtend equal angles as a rule, but it is not uncommon to find one subtends a greater angle than the other. This is commonly due to further relaxation of the fibular-collateral ligament by injury. When the condition is unilateral it is always the result of injury, but it can only be said to be unilateral if a check examination of the opposite ankle is made under comparable conditions. Attempts to produce hypereversion of the ankle under the same conditions have failed except in grossly injured ankles or in ankles which were the seat of old injury as shown by the presence of an ununited fragment of the medial malleolus.

Significance of the hypermobile ankle.—Such an ankle, unless controlled by a well-developed leg musculature is extremely liable to minor sprains and twists. Indeed it is the chief predisposing factor towards sprain and the causative factor in recurrent sprain. It may be stated that any sprain of an ankle of moderate severity, which recovers within a week, is probably a recurrent lesion. A moderate sprain of a normal ankle does not recover quickly and it takes three to four weeks before the joint feels strong again. Quick recovery should therefore raise suspicion of a recurrent lesion and will in a great number of cases be found associated with a hypermobile ankle. The hypermobile ankle is as frequently acquired as hereditary. Its acquisition (in which case it is usually unilateral) is due in the vast majority of cases to neglect of a sprain. This may be either failure to diagnose a rupture of the fibular-collateral ligament when present or neglect of repeated minor injuries at sport. The injection of local anæsthesia, or the abolition of pain by the freezing method is fraught with danger if the surgeon has not taken steps to assure himself that there is no complete rupture of a ligament. This may be assessed with considerable certainty by experience in the normal foot, but is rendered more difficult in the patient with hypermobile feet. In such cases, in order to establish an accurate diagnosis radiographs of both ankles should be taken under intravenous anæsthesia. It is true that rupture of a collateral ligament may be shown by inversion strain under local anæsthesia (Hughes, 1942), but the pictures are more accurately comparable under general anæsthesia, and less susceptible to error. A radiograph at right angles to the bimalleolar axis of the ankle is preferable to the true A.P. view.

ÆTIOLOGY

Bilateral hypermobility.—This is found in 4% of males, and 5% of normal females between the ages of 18 to 40 years (Tables A and B). It appears to be a congenital

MOBILITY OF NORMAL ANKLES.

Percentage mobility of hind-foot, estimated clinically	100 males, aged 18-40 years	TABLE A Cases with rotation of the talus in ankle-joints. X-ray controlled. Degree of tilt	100 females, aged 18-40 years	TABLE B Cases with rotation of the talus in ankle-joints. X-ray controlled. Degree of tilt
Hypermobile { 100 / 90 / 80	—⎫ 5 ⎬13 8⎭ %	15, 5, 8, 10	—⎫ 11 ⎬26 15⎭ %	5, 5, 5, 8, 10
Mobile or Normal { 70 / 60 / 50 / 40	4⎫ 0 ⎪ 21 ⎬59 25⎭		18⎫ 26 ⎪ 14 ⎬71 13⎭	
Rigid { 30 / 20 / 10 / 0	18⎫ 9 ⎬25 1⎭		2⎫ 1 ⎬3 —⎭	

Tilt expressed in degrees. All observations without anæsthesia. Figures refer to both ankles. Five cases with unilateral hypermobility were found in examining each sex; all gave a history of injury and were excluded, making 105 cases in all examined of each sex.

condition, which is not due to any alteration in the bony configuration of the ankle, but to ligamentous laxity. It shows little relation to the general build of the patient. It predisposes to sprains of the calcaneo-fibular ligament, the anterior talo-fibular ligament and the midtarsal sprains. The degree of mobility of the ankle-joint can be retained or increased by active exercises, as in ballet dancers, where the excellent muscular control offsets the tendency to sprains. In athletes following a series of minor sprains both ankles may become relaxed, but it is highly probable that such ankles were hypermobile to start with.

Unilateral hypermobility.—In the examination of cases to obtain figures for 100 normal

ankles it was found that five cases of each sex showed unilateral hypermobility and these all gave a history of injury, and so were excluded from the tables. This gives some idea of the frequency of its occurrence in the ordinary population. In acute sprains it was present in eight out of the fourteen sprains of the calcaneo-fibular ligament examined radiologically, the remainder showing hypermobility of both ankles (Table C). The common injuries predisposing to the conditions are: Rupture of the calcaneo-fibular ligament; or rupture of the calcaneo-fibular and anterior talo-fibular ligaments. Sprain of the anterior talo-fibular ligament is in our experience most commonly associated with sprains of the calcaneo-fibular ligament (inversion) and rupture of the anterior fibres of the deltoid (plantar flexion). If it occurs as an isolated lesion it is doubtful if it allows any twist of the talus to take place and then only if the foot is in plantar flexion. Rupture of the tibio-fibular syndesmosis or fracture may result in opening up the mortice to a slight degree, but if the calcaneo-fibular and anterior talo-fibular ligaments remain intact inversion remains unaffected.

Rupture of the fibular-collateral ligament.—It is extremely doubtful if this ligament often ruptured in its entirety. It is probable that a tilt of the talus of 45 degrees (usually described as a dislocation of the ankle) can occur following rupture of the anterior talo-fibular ligament and the calcaneo-fibular ligament alone. The peculiar course of the posterior-talo-fibular ligament, which forms a separate entity makes it likely that such rotation rather than stretching it, would relax it. It is thus incorrect to speak of ruptures of the fibular-collateral ligament unless this term is used to describe the anterior and middle band of the external lateral ligament only, and it is used in this sense in Table C.

Rupture of the calcaneo-fibular ligament.—This ligament is the most important single ligament opposing inversion of the hind-foot and its rupture or relaxation the most common cause of hypermobility of the ankle. It is inevitably relaxed in ruptures of the fibular-collateral ligament but it is more commonly ruptured alone. Frequently the relaxation is due to a sprain fracture of the tip of the fibula, rarely to a pulling out of its attachment to the calcaneus. The ligament controls movements at both the ankle-joint and at the subtaloid joint and the increased inversion following its rupture occurs at both joints, though the ankle-joint is relaxed to a greater degree. In recurrent sprains of the ankle the damage to the ligament is often shown by the presence of a small fragment of bone below the fibula. Increased mobility of the ankle-joint predisposes particularly to this injury (Table C).

TABLE C.—ANALYSIS OF EIGHTY SPRAINED ANKLES (MEN 18-40 YEARS).

Ligament	Hypermobile Hind-feet (42·5%)			Mobile Hind-feet (51·25%)		Immobile hind-feet (6·25%)	Per cent age
	Clinically diagnosed	Radiologically confirmed (ankle only)		Clinically diagnosed	Radiologically confirmed		
Fibular-collateral	2	45, 35 / 10, 5		1	45 / X	—	4
Ant. tibio-fibular	6	X, 5 / X, 5		17	X, X, X, X, X / X, X, X, X, X	2	31
Calcaneo-fibular	13	20, 20, 15, 10, 10, 15, 20, 12, 10 / 5, X, 10, X, 5, 10, X, 5, 5		6	5, 20, 8, 10, 10 / X, X, X, X, X	—	24
Ant. talo-fibular, alone	3	5 / 5		2	X, X / X, X	—	6
Deltoid. Complete	—	—	Negative X-ray findings indicate mobility confined to subtaloid and midtarsal joints	1	45 (eversion) / X	—	1
Ant. fibres of deltoid with ant. talo-fib.	3	10, X, X / 10, X, X		3	X, X / X, X	1	9
Deltoid. Partial	1			2	5, (eversion) X / X, X	1	5
Midtarsal sprains	4	20, 10, 10 / 20, 10, 5		5	X / X	1	12
Undetermined	2	—		4	X / X	—	8
Totals	34	20		41	20	5	

The figures above the line are for the injured ankle; those below for the corresponding opposite ankle. Twist of the talus expressed in degrees. X = no twist. All radiological observations under pentothal.

...le of the ankle-joint.—Following excessive activity in athletes, ...otballers, abnormally mobile ankles are often found. There ...ated minor trauma and radiological evidence of sprains in fractures or scattered ossification in a ligament. The con- "athletes' ankle" is characterized by a small exostosis on ...lus, visible in the lateral radiograph and due to repeated hyperflexion of the ankle. Later on evidence of mild ...ically and complaints of aching after use, tiredness,

and susceptibility of the joint to damp, appear. The general ligamentous relaxation is particularly obvious in the fibular-collateral ligament allowing increased inversion.

Statistics.—An endeavour to estimate the mobility of the hind-foot on both sides in cases of sprained ankles was made, first as part of the radiological examination of badly sprained ankles, and then when it became apparent that this bore some relation to the type of sprain and to the liability to sprains, in all cases of sprain. Unfortunately in the earlier cases this was expressed as mobile, hypermobile, and rigid, and not as a percentage estimate of mobility, which was found to be much more convenient. As a standard the ankles of 100 normal males (18 to 40 years of age) and 100 normal females of the same age-group were examined. The mobility of the hind-foot in women is considerably greater on the average than in the male, a fact which corresponds to the generally greater ligamentous laxity found in women. When the eleven clinically hypermobile ankles (Table B) were examined only five of these showed a relaxation of the fibular-collateral ligament, thus suggesting that the increased mobility was mainly in the mid-tarsal and subtaloid joint and not at the ankle. On the other hand all the males but one who showed hypermobility of the hind-foot showed some rotation of the talus and it is possible that the exceptional case might have done so under anæsthesia. This confirms the opinion that in the male excessive inversion of the foot is accompanied by a relaxation of the fibular-collateral ligament. It was necessary to find if a relation between this fact and the incidence of sprains existed. Accordingly all sprained ankles were carefully examined and the site of ligament damage noted, and against this the mobility of the foot on the opposite side was marked. In serious cases radiological control was used and both ankles radiographed in inversion under pentothal anæsthesia. The results are shown in Table C. It will be seen that sprain of the anterior tibio-fibular ligament is the most common sprain of the ankle (31%). This occurs from external rotation violence and reflects the frequency of this type of injury as a cause of fracture around the ankle. This movement is not related to the mobility of the hind-foot which cannot influence this type of sprain. It is primarily lesions of the fibular-collateral ligament or its components which the increased inversion of the heel facilitates by increasing the power of the lever provided by the depth of the calcaneus. Accordingly we note a marked preponderance of these injuries among the hypermobile ankles—where they form 66% of the injuries compared to 33% of the normal male ankles. When the relative proportion of hypermobile to normal ankles (13% to 59%) is considered this emphasizes the proportion still more. It must be borne in mind, however, that a certain percentage of the fibular-collateral ligament sprains occurred in previously injured ankles, the tendency to recurrence thus increasing the apparent proportions among this section. Abnormal flexibility of the hind-foot also predisposed to sprains at the midtarsal joint.

A striking fact is the absence of sprains among the patients with rigid feet. It has not yet been possible to determine whether this is offset by a higher percentage of fractures in these ankles, but this seems highly probable. Unfortunately no comparative series of sprains in women was available. They are more predisposed to sprains by virtue of the increased flexibility of the hind-foot and the higher heels of their footwear, but this is offset by the sporting and occupational hazards of the male to which most sprains are due.

TREATMENT

Preventive.—Adequate investigation and immobilization of sprains—which includes radiographic examination of all severe sprains under inversion strain, and comparison with the opposite side.

Prophylactic.—The development of adequate muscle control may not always be possible, but in athletes the peronei may be developed by exercising them against resistance. This can be accomplished by the use of a shoe with a weight attached to the outer side of the sole and running over a pulley, lying to the medial side. Eversion is then practised against weight resistance.

In women the tendency to inversion is encouraged by wearing high heels. Lowering the heel and broadening the base is first tried. If this fails the heel may be floated out, though most women object to the appearance of this alteration. In men broad and low heels are already being worn. Boots for rough work may assist the patient. Wedging the sole and heel 3/16 in. on the outside may prevent the foot turning over so easily. In athletes the support of a properly applied bandage (figure of 8 over the external malleolus) or even of strapping is of great assistance during a match. In cases where it is imperative that the patient should continue to run a risk of spraining a hypermobile ankle, to earn his livelihood, special boots with thin steel stiffeners in each side should

be worn. The strength of the steel and the height of the boot is adapted to the patient's build and activity.

SUMMARY

The mobility of the hind-foot is very variable, being greater in women, and depending on the mobility at the ankle, subtaloid and midtarsal joints.

In cases with hypermobility of the hind-foot this may be due to excessive movement at all joints, and a twist of the talus of 5 to 25 degrees in the tibio-fibular mortice may be shown radiologically, in 4% to 5% of normal people.

In some cases the hypermobility is confined to the subtaloid and midtarsal joint and this is more common among women.

Hypermobility of the ankle produces a feeling of instability, complaint of "going over" and recurrent sprains.

Hypermobility is a prime factor in the incidence of sprains of the fibular-collateral ligament or its components.

Severe sprains of the calcaneo-fibular ligament are a primary cause of unilateral hypermobility.

Simple preventive measures are described.

REFERENCE

[HUGHES, J. R. (1942) Sprains and Subluxations of the Ankle-joint, *Proc. R. Soc. Med.*, 35, 765.

Mr. R. G. Pulvertaft showed a short film illustrating **Tendon Suture of the Hand.**

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[January 20, 1944]

Cases of Chloracne (See-kay Wax).—J. E. M. WIGLEY, M.B.

Two girls, aged 15 and 21 years. One married and one single.

They have been employed during the past eighteen months in a part of a "condenser manufacturing" factory where the essential work was the dipping of various parts in heated molten See-kay wax. Neither of these girls directly handled the dipping process but they were employed in comparatively close proximity to it, and the girl with the more marked affection appeared to have the less possible contact with the molten wax.

The parts affected were the hair margin, the forehead, the cheeks, and lobes of the ears. The eruption consisted of large numbers of comedones. many yellowish-white, shiny papules (resembling sebaceous cysts), a few pustules and, on the cheeks, some mild underlying erythema.

Symptoms were slight, though there was some irritation, and the principal complaint was of the disfigurement.

See-kay wax consists of a chlorinated naphthalene and closely resembles the halowax referred to by Good and Pensky (C. K. Good and N. Pensky, 1943, "Halowax Acne", *Arch. Derm. Syph.*, 48, 251).

Dr. I. Muende: About eight years ago I had the opportunity of examining some 120 girls who had developed chloracne whilst working with different chlorinated naphthalene waxes. The cases were, on the average, very similar clinically to those shown by Dr. Wigley although some had their lesions more widely distributed, not merely on the face and ears but also the forearms, thighs, trunk and genitalia. It was at one time considered to be due to irritation from without but it was my view that it was produced as a result of inhalation of the fumes. I was interested to note that workers usually found that their appetite was very considerably increased, to a greater extent than would be expected as a result of the physical energy expended, and when asked what their appetite was like, usually replied "It is very good, I eat like a horse". Oddly enough, Dr. Wigley's patient gave precisely the same reply. Further, the skin almost always becomes hypersensitive to light, the patients complaining of severe burning when exposed to the sun. Patch tests always proved negative and urological examination was not helpful. Sections were prepared from typical lesions and the histological appearances simulated those of ordinary acne but, interestingly enough, the comedones appeared to be relatively free from organisms and cultures were always negative. This seemed to point to the sterilizing effect of the substance whilst being excreted through the sebaceous glands. One of my cases who developed jaundice died later of acute yellow atrophy. Since then several similar cases have been reported in America. Experimental work on guinea-pigs which were given sublethal doses of carbon tetrachloride and subsequent administration of the chlorinated naphthalene by the mouth resulted in necrosis of the liver. Besides the mono-, di-, tri-, tetra-, penta-chlorinated naphthalenes, di-chlor-di-benzol is apparently capable of producing the same eruption.

Dr. Kenneth J. M. Graham: One factory I visit is engaged in plating, chiefly armament for torpedo boats which has to be proof against sea water and needs a thick deposit. Sometimes the wax is used when it is required that one end of an article shall remain ordinary steel and the other end be plated. Other waxes have been tried but have not been found satisfactory. In this factory the proportion of quite badly marked cases was 20% and there would be a further 25% of transient lesions of a similar kind in people who are in fairly close contact with these others but not actually working in the wax.

I have regarded this condition of wax acne as due to the mechanical blocking of certain follicles with the actual wax and thought the pustule effect was secondary infection with staphylococci so I used a staphylococcal vaccoid on the workers, with good results. Ten doses from 0·1 c.c. rising to 1 c.c. were given. Later, in selected cases, I gave another course. In addition I have given hot fomentations three times a day by means of hot towels over the face. I do not know whether the improvement was entirely due to the vaccoid or to the fomentations.

The Government had a few extractors put over the vats but the vaporized wax went up the duct and condensed so that there was a solid block of wax at the top of the pipe. This is now cleared weekly and conditions have improved. Recently the flooring round

the vats has been kept much cleaner and this seems already to be causing a decrease in the severity of the acne.

I have had only two men temporarily suspended. Very often after three or four weeks the condition clears up when away from work. I have not seen any sign of acute yellow atrophy or jaundice. Blood-counts were normal and the workers do not remark on an increase of appetite.

Creams do not seem to do any good. Ordinary zinc ointment does as much good as proprietary preparations. I have often given 10 gr. menthol in 2 oz. zinc ointment, which has a cooling effect.

The condition can come under scheduled diseases. It is obviously due to the industry and there is a certain amount of secondary dermatitis attached to it. We can call it Industrial Dermatitis if we will and workers can claim compensation for as long as they are out of work. They cannot get other employment while they are disfigured.

Some of these men who had lesions about three years ago are permanently scarred as if they had smallpox, but they do not appear to mind their personal appearance. I have had very few suspensions. One reason may be that they are paid extra for this work and are a good set of employees.

Dr. J. E. M. Wigley: I visited the factory with Dr. Graham where I found the First Aid Post, consisting of a small room with an ordinarily fitting door, was about 15 to 20 yards away from the vat containing the molten wax. Over the vat was the fume extractor. The nurse remained most of the time in her First Aid Post, seldom going to the vat, and had been employed there for about twelve months. I noticed that there was definite evidence of an acneiform eruption, with comedones, on her malar prominences. This would appear to confirm the view that the chloracne is caused, principally, by contact with the vapour arising from the molten wax.

The results of patch tests, reported by Good and Pensky, were consistently negative.

Dr. H. C. Semon: I remember a severe case of chloracne, one of several, which occurred among a group of electricians working with so-called "flame-proof wire", some six years ago. Except that the points on which they were working were in a confined space, where the ventilation was defective, there was nothing abnormal in the environment. I discovered that chlorinated naphthalene was freely used in the construction of the insulating material, and shortly afterwards Dr. Haldin-Davis published a comprehensive report on a series of identical cases (*Brit. J. Derm.*, 51, 380-3). "These men (10) were all employed indoors in pulling wire covered with chlorinated naphthalene through conduits which were above their heads, and this process resulted in the detachment of fine particles of the coating, which fell on their heads and necks, and also upon their forearms. As only these parts showed evidence of the eruption, it is quite possible that it was caused by the actual dust and not by an exhalation from the chlorinated naphthalene".

Possibly too, the reason that men working out of doors largely escape similar ill-effects is that the particles of dust, if present, do not settle on the skin, but are blown away.

As Medical Referee quite recently I saw a case claiming compensation under the W.C.A. I had no hesitation in deciding, as I have done on several previous occasions, that the condition was compensable under Workmen's Compensation' (Industrial Diseases) Order, 1941—Poisoning by chlorinated naphthalene or its sequelæ—cp. Willis's W.C.A., p. 716: "Any process involving contact with or exposure to dust or fume of chlorinated naphthalene." So far the decision has not been called in question, although it cannot be said the workmen were actually disabled from earning full wages by reason of the stigmata produced.

Major W. J. O'Donovan: In addition to what Dr. Muende has just said about the sensitiveness of these acne patients to light, they may become extraordinarily sensitive to soap and water and other things. One point to be borne in mind is the disfigurement caused by the condition. In times of peace one advised the affected workers to give up their noxious employment. I did not then know that cure was so rapid as is related to-day. Do these workers ordinarily receive compensation? Has the question ever been decided in court whether or no any compensation can be drawn for these cases? They do not suffer from disabling dermatitis. They could indeed plead that they are unfit to follow the occupation of a manicurist, of perhaps of a hairdresser's attendant, but they are fit for other female labouring work. I have this difficulty in mind, namely that this disease is not dermatitis produced by dust and liquids, more particularly so if the contention advanced by Dr. Muende that it may be produced by inhalation of gas or vapour holds the field. The causation of chloracne has been in dispute since 1889.

Necrobiosis Lipoidica Diabeticorum (Urbach).—A. Murray Stuart, F.R.C.S.

Mrs. T., aged 46. She has suffered from diabetes mellitus since 1936 and has been under continuous insulin therapy, averaging about 40 units zinc, 20 units soluble, daily.

Her fasting blood sugar on 8.11.43 was 186 mg.%.

Skin lesions first appeared in August 1943 and have since increased in number. She now shows indurated intradermal papules on the left forearm, right buttock and upper part of the left thigh. She had a plaque on the left thigh which was excised for histological examination. The scar shows some of the characteristic changes. Sections show subepidermal necrotic areas surrounded by histiocytes with some giant cells. There is fat in the necrotic areas and in the cytoplasm of the histiocytes.

An interesting point, to my mind, is that I believe all reported cases have been under

insulin treatment. The first recorded case, I think, was by Urbach in 1932, at about the time—or soon after—insulin was first started. Is it possible that the treatment has something to do with the causation of the condition?

Dr. Robert Klaber: The suggestion that insulin may play some part in exciting this condition was not borne out by the first case which I showed to this Section in which the diabetes itself was not diagnosed until some years after the lesions appeared, so that the patient had previously had no insulin at all (*Proceedings*, 1933, 27, 713). The skin lesions in that case cleared up rapidly when her mild diabetes was controlled by insulin.

Case for Diagnosis. ? Staphylococcal Eruption.—H. J. WALLACE, M.R.C.P.
G. P., male, aged 23.

The eruption, which has been present for five weeks, began as solid nodules in the skin distributed all over the body and varying in size from a pin's head to a hazel nut. At no time has there been any irritation or constitutional upset. The lesions varied in colour from yellow to intense red and in the largest of them central necrosis and suppuration was beginning. There is no history of ingestion of bromides or iodides.

The condition has been treated with antiseptic baths and sulphathiazole cream locally and is now gradually regressing.

He is a gunner in the Merchant Navy and has recently returned from America. He has seen much tropical service. There is nothing relevant in his past history. He has been in hospital for the past four weeks and has been afebrile throughout.

Culture of nodules grew *Staphylococcus albus* only. Blood Wassermann reaction negative. Blood-count normal.

Histology.—The biopsy of a nodule from this man's skin showed infiltration of the whole of the corium with inflammatory cells in which histiocytes predominated but with a fair number of plasma cells. There were local areas from which collagen had disappeared.

The President: He had a few lesions on the anterior axillary folds, some of them not unlike the extraordinarily indurated lesions which may last for months after scabies.

Lepra Maculo-anæsthetica.—HENRY HABER, M.D. (*introduced by* Dr. GEOFFREY DUCKWORTH).

Cypriot, aged 33, who came to England in August 1939. Syphilis twelve years ago. First symptoms of leprosy in 1940 when a slightly itching rash appeared on the hands and feet. During the following year similar lesions developed on the chest and trunk and later on the face. Six months after this, areas of anæsthesia were discovered (hand, ankles, left temple, forehead and chest). Nose bleeding occurred two years after the appearance of the first symptoms.

Present condition.—Striking alopecia of eyebrows and eyelashes. Brown nodules showing slight desquamation on the face which has the appearance of acne rosacea; there are also nodules on both arms and ears. Brownish slightly scaling macular rash on abdomen and back, some of the lesions resembling parapsoriasis. The hands and feet are acrocyanotic and the skin slightly atrophic. There is a sloughing ulcer surrounded by smaller ones on the left leg. Both ulnar nerves are thickened. Nasal smear shows the presence of Hansen's bacilli.

Biopsy.—Chronic inflammation in stratum papillare and sub-papillare. Ziehl-Neelsen stain shows Hansen's bacilli. Wassermann reaction negative.

This is the second case of leprosy in a Cypriot which I have seen in three months at the Lock Hospital.

The President: It is rather striking that we have had two cases of leprosy at consecutive meetings, and I have had a third case out at Wellhouse, who contracted it in Nigeria. He was in that country for fifteen years and developed it just as he was leaving. Apparently he had had it for two years in this country without being detected. What is the incidence of leprosy in Cyprus?

Dr. Haber: I started investigating the other Cypriots at the Lock Hospital, but all were negative for leprosy.

Tuberculosis Verrucosa Cutis.—Henry Haber, M.D.

Male, aged 57; a post-mortem attendant. A papular lesion appeared on the back of the left hand sixteen months ago. He uses gloves only occasionally.

On examination.—A verrucous patch with typical blue border. Two small lesions on right wrist.

Histology.—Hyperkeratosis and acanthosis. Chronic purulent inflammation due to pus cocci.

Wassermann reaction negative. X-ray photograph of chest showed no changes. No actinomyces could be grown.

The President: Is it not usual to get some tuberculous structure in tuberculosis verrucosa cutis?

Dr. I. Muende: The histological changes present in sections of tuberculosis verrucosa cutis differ not merely from case to case but also occasionally from different areas in the same lesion. The marked acanthosis and hyperkeratosis are always present but the inflammatory infiltration in the upper part of the corium may reveal the presence of either (a) densely packed lymphocytes, (b) lymphocytes with a few centrally placed endothelial cells, or (c) lymphocytes, endothelial cells and giant cells. Only rarely does one find anything approaching a typical tubercle system.

In tuberculosis verrucosa cutis there is no destruction of tissue leading to liquefaction and accumulation of pus, whereas in non-tuberculous pyoderma the lesion, which is always deeper, is necrotic if not actually liquefied, and polymorphs and pus cells are present.

Major W. J. O'Donovan: There is a social responsibility attaching to this diagnosis. Sixteen years ago I had a case in a man who was the proprietor of a suburban milk shop. One felt compelled to notify this tuberculosis cutis, and as a consequence he had to abandon his business. In a case of leprosy no one would question such a decision, but in lupus I wondered whether I was right in agreeing with the Medical Officer of Health that the man should abandon the milk trade. The lesion was on the back of his hand, and the communicability of lupus is very disputable.

Dr. Louis Forman: This case reminds me of one shown by Dr. Klaber (*Proceedings*, 1933, 26, 750) of actinomycosis.

The history is a short one for tuberculosis, and the granulations are softer than one would expect.

Dr. Semon: In my experience these cases are usually associated with lung changes or hilum changes.

Neurotic Excoriations and Epithelioma.—Henry Haber, M.D.

Girl, aged 20 years, clerk.

In an otherwise healthy girl there developed a slight acne eruption on the face, four years ago.

The patient could not help picking the lesions and some secondary infection and scarring developed on the nose. She has been treated on routine lines with lotions and sedatives. During treatment she developed within six weeks an epithelioma about the size of a silver threepence on the right temple. She states it was preceded by a small pustular lesion and there is no evidence of a pre-existing mole. Treated by unscreened radiation for one and a half hours at Mount Vernon Hospital. W.R. negative.

Dr. J. H. Sequeira: I recall seeing this condition on the back of a boy of 11. I also saw it on the lower eyelid in a young girl of about 18. Her case was interesting because she was the only person who looked after her grandfather, who was a patient in my department for extensive rodent ulcer. I put the facts before the late Sir Henry Butlin, who at that time was taking great interest in carcinoma of the skin, but he refused to accept it as a case of "implantation" cancer. The small boy with the lesion on the back was cured by X-rays, and the girl by radium. The latter was in 1902.

The President: The woman in this case has been treated with unscreened radium. My own experience as well as my observation of cases which have in the past been treated in that way is that unscreened radium is not anything like as good for the treatment of rodent ulcer as thoroughly screened radium in which only the gamma rays are used.

Dr. Haber: It depends very largely on the type of lesion. If there is any suspicion of attachment to underlying tissue or if there is rather deep ulceration, treatment with screened radium may be better, but one cannot be dogmatic as to the merits of screened or unscreened radium in the treatment of rodent ulcer.

JOINT DISCUSSION No. 2

Section of Dermatology with
Section of Epidemiology and State Medicine

Chairman—A. C. ROXBURGH, M.D.
(President of Section of Dermatology)

[*December* 16, 1943]

THE ORGANIZATION OF THE TREATMENT OF LUPUS VULGARIS

Dr. F. S. Airey : I believe we have no true conception of the incidence of lupus in this country; its distribution; the facilities available for its treatment; their adequacy; the extent to which those afflicted avail themselves of the opportunities for treatment, and the success of the measures adopted.

(1) The incidence of lupus in the various parts of this country should be ascertained. Stühmer has given us the figure of one case per 1,000 of the population. If we accept this figure for Britain we have 45,000 lupus cases. Only a census can show if this estimate is correct. There are many parts of this country where lupus is neglected. Because we are unaware, we act as if we were unconcerned.

(2) Facilities for treatment should be examined and classified. Some may be satisfied with the facilities which exist in London and the large cities, but I am concerned about the rest of Britain, where I have seen sufficient to believe there is a lupus problem and that facilities are poor. Only an examination of existing facilities, followed by classification, can show the true state of affairs.

(3) Revised and adequate facilities should be provided. We cannot assess our requirements until we know the incidence and the distribution of the disease, and the quality of existing facilities for treatment. Some project on a national scale is urgently required. We have a lead from Germany and Russia. Diagnosis stations can be established; some network created to link together treatment centres; some means of ensuring continuity of treatment for the patient and, particularly, some way of assuring him of a "square deal". Instead of waiting until the patient comes for treatment we must seek him out, and put him in touch with the appropriate vital centre.

Local and general light therapy for ambulant patients are necessary aids, without which it is doubtful if we can achieve our object. We must extend and improve existing facilities. (There are still places where it is customary to direct an open mercury vapour lamp at a patch of lupus from a distance of a foot or two and call it local therapy.) I know what good work is being done in some places but what treatment is being received by the 40,000 of our 45,000 (estimated) cases?

Ambulant treatment is insufficient in some instances. Institutional therapy has much to commend it and provision must be made for it on a proper scale.

(4) By propaganda the social conscience can be awakened, and the lupus sufferer found and relieved. Activity on a national scale must characterize our efforts in the future. We must raise the standard of the many to that which at present is achieved by a few. Just as the Public Health Authorities have tackled diphtheria, so must we, by propaganda, persuade the sufferers to present themselves for treatment at an early stage. Similarly, by professional propaganda, the general practitioner should be made aware of modern advances in treatment and the improved facilities available.

(5) Unified control should be established with a national system of record-keeping. Unified control, with the establishment of a central bureau, is our best chance of success. It could act as a sorting-office for records and information, facilitating follow-up and

transfer. Danbolt has such a control centre in Oslo; it is simple, but impressively adequate. Let us hope it is still in action.

(6) Information on technical matters should be made readily accessible and research encouraged. From such a central bureau would come stimulus to peripheral workers. The latest methods should be examined, tested and made known. With Europe so disturbed, surely it rests with us to maintain the high endeavours of others now severely hampered in their task, though in this field I am not overlooking the valuable work of British physicians.

In 1934, at Bournemouth, Lomholt addressed an assembly of dermatologists. High hopes were expressed in the discussion which followed and, no doubt, efforts have been made. But we have not done much in the intervening nine years. Are we prepared to leave it at that or to proceed at our present slow pace?

I can see no other way of achieving success than to organize the control and treatment of lupus vulgaris on some such basis as I have described. Then we may see the disease coming rapidly under control. There is no real excuse for the present state of affairs. I, for one, am prepared to devote a good deal of time and effort to such a cause. Lupus vulgaris is a sociological as well as a medical problem and we must institute some machinery for dealing with the problem on the lines so admirably worked out already by our continental colleagues.

Sir Henry Gauvain (*in absentia* read by Dr. D. E. MACRAE): The treatment of lupus vulgaris is more neglected than that of any other form of tuberculosis. Though everybody knows that lupus vulgaris is a tuberculous disease, only very exceptionally are those measures, accepted as essential for the cure of tuberculosis, employed. Tuberculosis should be regarded as a general disease of which the local lesions are merely special manifestations.

Being a skin disease, though not uncommonly there are other manifestations, lupus is generally referred to the dermatologist, who has only the opportunity of treating the local lesions.

The Finsen-Lomholt lamp is very expensive. It cannot now be purchased, and spare parts cannot be generally procured in England; also efficient technicians are not readily available. One of the best technicians of the Finsen Institute spent a year instructing us at Treloar's Hospital, Alton. As Denmark is now in enemy hands, I believe it should be quite legal to undertake the manufacture of the Finsen lamps here and this should be done. If these lamps are essential, they should be readily obtainable at moderate cost.

While we should employ the Finsen treatment as indicated it is deplorable that it should have become a fetish. This has hindered research and has done much harm in often restricting treatment to areas where Finsen treatment is obtainable.

Possible lupus patients should be referred to centres scattered widely over the country where the disease could be accurately diagnosed and treatment at once instituted or the patient transferred to an appropriate centre. It is hopeless for treatment of early cases to be confined to a very few centres. The expense entailed and the upset in the patient's life make it impossible for this to be a practical or just procedure.

The disease usually, but not invariably, first manifests itself in childhood. Children are mentally much more sensitive than generally realized. When badly disfigured their distress is often acute and has a serious effect on their future outlook on life. They should be spared exhibiting their disfigurement to outsiders where possible. This entails admission to suitable residential institutions where treatment and education can be simultaneously given. This we do at Treloar's with the happiest results.

Even after apparent cure relapses are not uncommon. Such a relapse should be immediately treated, but, if a centre in the patient's neighbourhood is not readily available, most frequently nothing is done.

The patient remains untreated until so disfigured that continuance of employment is impossible. Out-patient treatment means that the patient has to travel in the company of others who resent his presence and often do not fail to make the sufferer aware of their disapproval. Moreover, unless he can continue in employment, cost of living has to be added to cost of treatment.

An attempt to solve this difficulty was made at the Lupus Hospital at Vienna where all possible members of the staff were, or had been, patients.

A lupus colony should be established for severely attacked adults. This should be in a secluded district with ample grounds and workshops. Here the patient could be treated and employed simultaneously.

I have established such a small colony entirely on my own responsibility without outside financial aid and its success has encouraged me to make further efforts. Accord-

ingly I have purchased a suitable house on an estate of 66 acres with ample workshops. This is now being adapted for the purpose intended.

Such a colony should be managed by a tuberculosis expert with experience in the treatment of lupus and who has made a special study of light therapy. He should be assisted by a dermatologist, plastic surgeon, rhinologist and laryngologist and should have all the facilities offered by a well-staffed hospital at his disposal.

A whole-time resident occupational therapist should supervise the employment of the patients. Social amenities should be readily available. At Morland Hall we have a social club much appreciated by the patients.

All the lupus patients at Morland Hall were so disfigured on admission that the only other practical way left to deal with them would have been admission to their local workhouse or public assistance institution. The oldest patient is 75 and was infected when aged 6. Practically the whole of her life has been clouded by the presence of this disfiguring disease. That this state of affairs should be remedied must be obvious.

Dr. Arthur Burrows : Dr. Sequeira and Dr. O'Donovan in their study of lupus vulgaris gave the cures with Finsen light treatment alone at about 60%, and showed how the addition of general light baths increased the successful cases to over 80%. Nevertheless there are a number of cases which for various reasons are not suitable for or do not respond to light treatment properly given. These cases should certainly have special consideration.

Small and localized patches of lupus are ideally treated at metropolitan or similar Finsen light centres. Regular attendance at frequent intervals for a considerable period is necessary. If travelling is convenient facilities for it can be provided; if not, extra centres might be instituted. There are of course other possibilities.

More extensive cases may be quite successfully treated by light but applications may have to be extended over a long period. These cases also need what again Dr. Sequeira and Dr. O'Donovan have emphasized, namely, *daily* general light treatment for months, not a perfunctory or limited course of two or three exposures a week. If these patients live near an adequate light centre and the economic side of the problem can be dealt with, all is well. Geographical, domestic and economic causes have definitely heretofore hindered the complete and satisfactory carrying out of light treatment in many cases. This also applies to patients with large widespread lesions and mutilation.

Many lupus patients suffer from phthisis and various other forms of tuberculosis. They are often unsuitable for general light treatment although Finsen-Lomholt can usually be used safely. Sanatorium or other forms of treatment may be called for under these circumstances.

Special training and assistance are necessary and must be available in dealing with lupus vulgaris in various difficult situations, as for example, when it affects the mucous membranes.

Complications such as the development of epitheliomata may need special attention, and I have not touched on the troubles which may arise through wrong diagnosis, an important factor which must be borne in mind in all organizations.

General skin clinics apart from light clinics have the great advantage of being inclined to try new forms of general and local treatment. Some treatments, e.g. excision of suitable patches, painting with acid nitrate of mercury although of limited application, are very valuable. The hydnocarpus esters or their relations warrant further trial. As a general treatment, my assistant, Dr. Warren, has obtained besides some failures, some promising improvements in bad cases of infiltrating lupus vulgaris. Here the organic chemist might be of great help. Such possibilities can only be explored in clinics where large numbers of cases are gathered together under a trained and varied medical staff.

The social and psychological side also needs consideration. In many cases lupus vulgaris can be treated while the patients are carrying on their ordinary lives, but the segregation of lupus patients has been advocated and in certain instances is certainly desirable.

Advantages of segregation.—Good food and hygienic surroundings are ensured. Dressings are done aseptically. The general health is looked after. The whole course of the reactions can be observed from day to day. The strain of long daily journeys is done away with. A certain amount of education or of training in various handicrafts could undoubtedly be given—as is done at Papworth. Special treatments could more easily and readily be given.

Disadvantages.—Patients of all ages and types create much friction and many small difficulties if herded together, and if the sexes are kept entirely separate it is very bad for the young adults. Even in the London Hospital out-patient clinic we have had a few cases of patients marrying each other and there would probably be many more

such marriages if patients are shut off from outside contacts. Many patients would refuse segregation, also separation may break up a happy marriage.

Psychologically the effect of segregation would be extremely bad. It would tend to make the patients feel they were unfit to mingle with other people. Also, when discharged, those who had suffered mutilation would find it more difficult to face the outside world than if they had never been withdrawn from it. Sister Cooper-Smith of the London Hospital Light Clinic, after living daily with lupus patients for twenty-three years is strongly of the opinion that the more they can be made to feel that other people can look at them without shrinking and the more they can lead normal lives the better. At the London Hospital we encourage them to move freely among their fellow men, to do their own shopping, carry on with their jobs, go to theatres, cinemas, churches and to share as far as possible in current events.

The L.C.C. started a small school for lupus children some years ago as an experiment. But even on this small scale great difficulties arose, chiefly from the difference in ages, ranging as they did from tiny children to girls and boys of 14. The results were so unsatisfactory that after a year the L.C.C. closed the school.

In cases with wide areas needing many applications the treatment is often a long and tedious one. This is one important factor in the organization of treatment, and another is total numbers.

From 1901 until the present year 4,153 cases of lupus vulgaris have attended the London Hospital Light Department. In the early years the numbers of new patients exceeded 100 annually and during the war period they have fallen as low as a quarter of that number but are now increasing again. There has been a tendency through the years to a slight annual diminution in the numbers of new patients. One of these reasons has no doubt been the formation of light clinics elsewhere, because the London Hospital Light Department draws its patients from all over England.

The annual number of Finsen treatments given is about 20,000 and the number of light baths between 30,000 and 40,000, except in war years. These numbers have been kept up even when the numbers of patients have declined, showing that more and more treatment can be given to individual patients with advantage when available.

Perhaps in due course the registration of lupus vulgaris cases will give us reliable figures. These numbers I have no doubt will seem insignificant beside those of some of our other national scourges.

Organization.—(1) *Ad hoc* centres with some residential accommodation for special cases for short periods. About ten such centres, new or founded on old ones, would be sufficient in England. (2) Arrangements to give patients periods in suitable sanatoria. (3) Provision for selected cases of lupus vulgaris in colonies for the tuberculous (not lupus only). (4) Facilities at sanatoria for advice and treatment of lupus occurring as a complication of other forms of tuberculosis. An experienced dermatologist should be in regular attendance on the lupus cases in these institutions.

Dr. F. R. G. Heaf: Lupus vulgaris is a comparatively rare condition, the treatment of which is long, expensive and highly specialized. The malady usually attacks the poorer classes and runs a chronic course, often causing disfigurement which prevents the sufferer obtaining employment even though the disease is cured. Organization for the treatment of such a condition is, therefore, not only a medical but also a social problem.

The comparative rarity of the condition is shown by the following figures:

TABLE I.—NUMBER OF NON-PULMONARY T.B. CASES IN WHICH TREATMENT WAS COMPLETED FOR THE FIVE YEARS, 1931-35, IN THE COUNCIL'S SPECIAL TUBERCULOSIS HOSPITALS.

	Quiescent	Improved	Unimproved	Died	Total
Lupus of skin	34	19	3	3	59
All N.P. sites	2,411	758	338	117	3,624

This gives an incidence of 1·63% amongst cases of non-pulmonary tuberculosis discharged or died during the period 1931-1935.

TABLE II.—NUMBER OF LUPUS VULGARIS CASES DISCHARGED FROM L.C.C. HOSPITALS DURING THREE-YEAR PERIOD, 1930-31-32.

Year	Adults		Children	
	Men	Women	Boys	Girls
1929-30... ...	2	4	2	—
1930-31... ...	2	7	3	5
1931-32... ...	1	5	—	1
Totals	5	16	5	6
	21		11	
	32			

I regret that the figures are incomplete, but many records have been destroyed by enemy action. More complete figures can be found in the annual reports of the Central Tuberculosis Officer for Lancashire (Dr. Lissant Cox).

TABLE III.—NOTIFICATIONS OF TUBERCULOSIS IN THE COUNTY OF LANCASHIRE.
(Taken from Annual Reports of the Chief Tuberculosis Officer, Dr. LISSANT COX.)
Population : 1,800,000 to 1,842,000.

Year	Total notifications all forms	Non-pulm. cases	Skin cases (Lupus)	Per cent. of N.P. cases
1932	2,302	825	48	5·8
1933	2,233	780	28	3·6
1934	2,059	744	37	5·0
1935	1,977	672	36	5·4
1936	1,970	722	31	4·3
1937			31	
1938	2,032	805	26	3·2
1939			26	
1940			35	
1941			26	
1942			15	

TABLE IV.—COUNTY OF LANCASHIRE. NUMBER OF CASES OF TUBERCULOSIS OF THE SKIN ON COUNTY DISPENSARY REGISTERS ON DECEMBER 31.
(Figures given by Dr. LISSANT COX.)

Year	Active	Quiescent
1933	230	165
1934	232	146
1935	224	124
1936	229	109
1937	226	92
1938	214	93
1939	221	85
1940	212	91
1941	197	93
1942	191	85

I have also searched recent Public Health Reports. The information on lupus is scanty. It would appear that either the incidence varies in different parts of the country or that the presence of a treatment centre is causing more cases to be discovered.

These figures give some indication of the magnitude of the problem and confirm my statement that the number for which accommodation should be provided is small.

TABLE V.—PUBLIC HEALTH REPORTS. FIGURES RELATING TO TUBERCULOSIS OF SKIN.
(LUPUS.)

Year	Authority	Population	Lupus New notifications	Lupus Under treatment
1940	Warwick and Coventry	424,710	—	5
1939	Staffordshire Jt. Board	970,700	3	—
1940			4	—
1941			5	—
1940	Northamptonshire	241,200	—	3
1940	Manchester	654,000	15	—
1941			17	—
1941	Glasgow	—	—	103 in 5 years
1940	York	98,050	—	9
1941			—	14
1936	Herts	474,700	—	20
1937			—	27
1937	Blackburn	126,900	1	—
1939	Oldham	124,400	2	—
1938	Southend	138,100	3	—
1942	Stoke-on-Trent	255,500	2	—
1942	Doncaster	72,140	—	18

This has an important bearing on diagnosis in that the disease is rarely seen in the medical schools and in any future schemes the maximum use should be made of known cases for teaching purposes, so that new cases may be discovered and treated in the early and easily curable stage.

As treatment is costly and needs specially trained staffs it should be located in centres which serve at least a population of 5 million. It is essentially a condition demanding regionalization and co-operation between local authorities to establish efficient treatment centres. In all probability the most convenient arrangement would be for the in-patient

centres to be attached to existing non-pulmonary tuberculosis hospitals and sanatoria with an out-patient and after-care clinic at the largest general hospital in the area. It should not be difficult to reserve a few beds for cases with open lung lesions properly segregated from other patients. I suggest these institutions for the special treatment of the active lesions because we must not only remember the intensive treatment of the lesion, but also provide adequate rehabilitation and after-care to rescue the individual with the extensive lesion from the ostracism which can cause such distressing social and economic conditions.

Children must be educated under conditions which will avoid their being teased and taunted because of their disability, and allow them to attend regularly for treatment with the minimum of interference with their studies.

I estimate that there are annually about ten cases of lupus per 1,000,000 population and that these will require 5 beds per 1,000,000 population with out-patient facilities to treat approximately 50 cases per 1,000,000 population.

Given the additional services of a dermatologist, rhinologist and a plastic surgeon, all of whom are essential members of the team, the majority of non-pulmonary tuberculosis institutions could provide accommodation for lupus cases. I say this because:— Usually they are already acquainted with the technique of light therapy. Operative procedures can be carried out at the institution. There are facilities for education and occupational therapy. There is usually a good system for after-care and rehabilitation.

Provision for this last item is of great importance when we look at the problem from the patient's angle. He is faced with the necessity for treatment which must be carried out seriously and continuously, adhering conscientiously to the instruction of the dermatologist for a period varying from two to twelve months, during which time he will be unemployed. He is probably poor and needy when diagnosed and, unfortunately, unless he has a pulmonary lesion cannot receive financial assistance under Memorandum 266T. Public assistance will have to come to the rescue but it would be better still if he could be provided with remunerative useful work. This should be done on the lines so successfully developed at Alton and Oswestry, or failing that it should be possible to provide work on the staff at the treatment centre.

If there is considerable disfigurement permanent residence at an industrial settlement like Papworth will have to be considered when the activity of the lesion has been overcome. To deal with the lupus problem I therefore suggest: (1) Close connexion with the medical schools be maintained to ensure that students and practitioners are able to diagnose the lesion in its early stages. (2) Special treatment centres be established with in-patient accommodation at non-pulmonary tuberculosis hospitals. (3) Adequate facilities for after-care, vocational training and colonization be established. (4) The tuberculosis allowances be extended to include these cases so that they may undergo treatment without financial embarrassment.

Dr. Henry MacCormac said that he was under the impression that tuberculosis of the skin was a notifiable disease, as were other forms of tuberculosis. Therefore there should be available some official record of the total number of cases. He believed, with other speakers, that it was an extremely rare disease, though that was no good reason for neglecting it. Every dermatologist was aware that the difficulties of dealing with this condition were economic rather than therapeutic. He had been struck by the fact that many patients suffering from an early degree of lupus got quite well following the standard out-patient routine. If these cases were recognized sufficiently early they could be treated at that stage, with a much enhanced prospect of cure. To try to regiment people and put them into an institution would open up many difficulties. At the same time, it seemed to him that something similar to what was done in Denmark might be established here, namely, to provide the patient with a means of livelihood while attending the centre. Occupation was a very important thing for these people.

Lupus had a geographical distribution. It was common in Scandinavian countries, it was found in Great Britain, but, as he had been informed by his Australian colleagues, was almost unknown in Australia; all the Australian cases were imported. The best therapeutic results had in his experience been observed following treatment at Leysin, where the patient was exposed to the sun in the high Alps and where, in consequence, lupus improved enormously even after three or four months.

Major W. J. O'Donovan, speaking with regard to the size of the problem, said that if lupus vulgaris had been neglected, then the review of man-power in this war carried out by the National Service Boards would have shown up the neglect. If there were revealed in these examinations by medical boards one in a thousand past or present

sufferers from lupus, the fact would by now be clamant. In the whole of a Command in the Army, covering one-quarter of this country, from which since the beginning of the war all dubious skin conditions had come to him, he had seen only four cases of lupus vulgaris, and those were slight. If a census was proposed it must be remembered that much lupus was not on the face, and working people were not too keen to expose those parts of the body usually covered, as those concerned in the public health were well aware.

If it were a small problem he would confirm what Dr. Burrows and Dr. Heaf had said that it was also, before this war, a diminishing problem in southern England. As far as organization went, the most important thing was the prevention of lupus, and that was proceeding through the greater care of the public health, meat inspection, and also abolition of smoke (Smoke Abatement Act, 1926). He paid a tribute to the work of school medical officers throughout the country. When he first began to assist Dr. Sequeira at the London Hospital there was a multitude of horrific cases which, in pictures, appealed to the crisis-minded, but as the years went on there was a gradual diminution in these cases, and an increase in the number of cases sent early by school medical officers. The L.C.C. in those days sent its school medical officers to study the clinical signs of lupus under Dr. Sequeira at the London Hospital, and that piece of foresight was an example of the well-organized care of lupus. The Sunlight League and organized tuberculosis officers had earned honourable mention.

He was glad that Dr. Airey had paid tribute to the powers of organization of doctors on the Continent. It might comfort them in their present distress to know that their good work in their own countries had not been unheeded. But it was also fair to say that in this country the medical profession had a great sense of organization. Speaking only for the London Hospital there had been a series of papers published since 1904 embodying changes in treatment as they had developed, and these could not have been published unless behind them was operating a sense of hospital organization, of planned staffing, of record-keeping, the use of photography, and so on. As the later papers showed, there had been the most willing co-operation of public health authorities.

In a paper published by Dr. Sequeira in 1925 it was pointed out that the Minister of Health had conferred ample facilities on public authorities in the shape of statutory powers to set up clinics and to finance the treatment of these cases. It was his experience that in the areas surrounding London these powers were fully used. He recalled the official publication by Dr. Lissant Cox in 1928 of some full and careful county statistics, clinical details, and financial costs of the treatment of lupus, including both initial costs and maintenance. A great deal had been done to stimulate the public authorities and to arouse the public conscience. An international Light Congress at Leysin in 1928 included an account of the work of Rollier on this subject.

After the war it was probable that lupus would increase. There would be difficulties of feeding, housing, medical education, and certain deficiencies in organization, but the one key to coping with the lupus problem had been mentioned that afternoon, namely the initial diagnosis. Here he must confess that it took him five years, during which he was seeing lupus daily in quantities, before he was positive as to the state of the skin of the patients under treatment.

Therefore the rapid erection of centres not preceded by a careful review of the state of medical education would give people a false impression of how the profession could serve them. Lupus was a simple and manageable problem. In the centres set out to deal with it one needed the assistance of other specialist colleagues. Treatment of lupus was expensive. It could be carried out under a skilled and experienced Sister with the assistance of a V.A.D. The treatment called for interest, concentration, and a study of one point of therapy only. At St. Louis Hospital, Paris, he had noticed that many of the nurses and hospital attendants suffered from lupus, and he thought that such people, if educated and courteous, and who had themselves been treated, would be the best people to persuade other patients to persist with the treatment.

Dr. A. M. H. Gray said that lupus was not a large public health problem, and therefore the matter had been rather neglected from that point of view. But as dermatologists they were interested in the human aspect of these cases, which was often distressing, and it was only right that some definite steps should be taken to deal with them.

He agreed with nearly all that Dr. Heaf had said both as regards the incidence of cases and also on the lines for the organization of treatment. When lupus occurred in children, they should be sent away to institutions which dealt with surgical tuberculosis and which were specially equipped. With adults a certain number obviously could not obtain work; others did not desire to do ordinary work for personal reasons, but would be willing to go into properly organized centres for treatment. The cases ought to be in

country surroundings, and treated on the same lines as the children, with the addition of occupational therapy.

For the rest there were a good many patients who preferred ambulant treatment. Dr. Heaf had suggested that this should be centred at the general hospitals, and particularly at the teaching hospitals in order that the students might see the cases and be able to make the diagnosis early and accurately. But in London with its twelve medical schools the number of cases appearing at each would be relatively small. The treatment required a highly technical department, and he doubted whether there was room for a properly organized department, like the department at the London Hospital, in every medical school in London. He would prefer to see the cases transferred to one or two centres' where treatment could be organized on a fairly large scale—a position which corresponded very closely to the view which was now prevalent of having only a few centres for radiotherapy. There would be always cases coming up for diagnosis, but the cases should be transferred for treatment to one or two hospitals with specialized departments.

One of the greatest advances of recent years was the tremendous improvement that could follow treatment by plastic surgery, and as a result there were a great many sufferers who were able to go back to work without any fear of what their neighbours might think. It would be a great advantage if the special treatment centres for lupus were in close proximity to plastic surgery units.

Dr. J. A. H. Brincker said that according to Lomholt the incidence in Denmark was about one in every thousand of the population. Thereupon investigations were started by the L.C.C., but as a result the new cases discovered in London were very few indeed. The medical officer arranged for one or more of the Finsen-Lomholt lamps at one of the L.C.C. institutions, but it took some years to get them. Generally speaking, they came to the conclusion that the two institutions where these cases could be conveniently treated were the London Hospital and at Treloar's Hospital, Alton.

Dr. J. T. Ingram said that in Leeds during the last fifteen years the total number of out-patients in the dermatological department of the Royal Infirmary had included 559 cases of lupus, working out at about one case of lupus per 4,000 of the population. Of those 559 cases, 138 for one reason or another had had no treatment, either dying, or refusing treatment. In other words, 75% of all cases submitted to proper treatment under this voluntary organization. Of the 421 cases treated, 324 had been apparently cured, and 175 of them had been cured for from five to ten years. The follow-up was very careful, and the cases were watched for a minimum of five years after all the treatment had stopped. What could be done was largely dependent upon an enthusiastic Sister and a good lady almoner, and the organization of the work in association with the local authorities. The West Riding County Council sent all their cases and paid their expenses, also contributing towards the cost of treatment. Among the adults, very few patients attended who were not working.

Of the 421 cases treated 27 were incurable. A colony would be a good thing for cases in that category, but apart from a small proportion of cases he did not think it was desirable. Great care must be taken before it was stated that a case of lupus was cured. The development of lupus depended not only on the tubercle bacillus but on other factors—psychological, nutritional, environmental. If a patient who had been cured returned to adverse social conditions he would relapse. Therefore after-care of these patients was important.

For economic reasons mercury vapour therapy had considerable advantages over carbon arc treatment. They owed an enormous debt to Finsen, but for economic reasons it was extremely difficult for lupus patients to give the time required for the treatment by carbon arc baths, and although he had four carbon arcs and four mercury vapour lamps and Finsen-Lomholt and Kromayer lamps, most of his results were obtained by means of light treatment from a mercury vapour source.

He agreed that it was essential to work with medical and other colleagues, especially the plastic surgeon and the ear, nose, and throat surgeon, and therefore this work should be at general hospitals where constant contact with one's colleagues was possible.

Surgeon Lieutenant-Commander H. R. Vickers, who was asked to contribute, said that during the last four years in the Navy he had only seen one case of tuberculosis of the skin.

Dr. R. T. Brain said that general treatment mattered quite as much as, if not more than, local treatment. Local treatment with light should be intense, and to ensure a maximum penetration local ischæmia produced by pressure is essential, but treatment

should not be limited to local applications. This brought forward the question of general ultraviolet light treatment. He was disappointed to find that having referred a patient with lupus to a suburban or provincial light clinic the patient was often told that only two or three treatments a week could be given and after twelve treatments two or three months' interval must elapse before resuming treatment. He could not understand that grossly inadequate technique. Of course, it was vitally important that the patient should have no latent phthisis, and it was customary to refer the patient for clinical and X-ray examinations of the chest before general light baths were given. The kidneys also should not be forgotten because renal disease might be aggravated by the intensity of irradiation. But, with these precautions, the patient should be given a very high concentration of ultraviolet light over a long period until the disease was cured.

He thought it would be practicable to devise a lamp like the Finsen-Lomholt at about one-tenth of its price.

Sir Weldon Dalrymple-Champneys (President of the Section of Epidemiology and State Medicine) said that he had learned much from the Discussion—much that it was important for the Ministry of Health to know. He entirely endorsed the remarks of Dr. O'Donovan with regard to the complete exoneration of the dermatologist.

The announced discussion was on the organization of the treatment of lupus, but everybody who had spoken had referred to the fact that the first thing was the ascertainment of the disease, and it seemed to him that they ought specially to bear that in mind. In a disease like this the incidence appeared to be unknown, but with regard to ascertainment he would have liked to have heard a little more about the competence of the general practitioner to make a provisional diagnosis of the disease. A great deal depended upon that. No one expected the general practitioner, except in the well-developed cases, to say definitely that a case was one of lupus, but it would be excellent if cases which hitherto had been ascertained only when they were fairly advanced could be discovered earlier, however small the total number of the patients might be.

It should be possible, he imagined, for a certain amount of extra instruction in this disease to be given to medical students in order that they might be trained to suspect a case as being early lupus and send it on to an expert to be diagnosed. He hoped very much that when a National Health Service was created in this country the general practitioner would become—as he suggested at some length in his recent Presidential Address to the Section (*Proc. R. Soc. Med.*, 1944, **37**, 89)—the real family doctor in the full sense of the word, with specialist skill and advice available when required. Under such circumstances he hoped that many conditions like lupus which had escaped notice would come to the surface, because the patient—or, if a child, the parents of the patient—would constantly consult the doctor, knowing that it was going to cost them no more, which was one of the advantages of a really universal health service. The doctor at that stage might be able to devise measures for preventing the condition from developing into fully-fledged lupus. Ascertainment and early treatment would thus be secured, and that would have the advantage of not requiring any special organization of lupus treatment, which in any case would concern only a comparatively small number of cases. These would be caught in the net which was spread to catch other diseases.

He gathered that financial difficulty was one of the reasons why patients did not get sufficient treatment. Was it also the cause of late diagnosis? That again, he felt sure, would be one of the things which would be remedied in a national service. He did not believe that the people of this country would be content with a universal health service which did not take cognizance of and deal effectively with that very point. The financial question was one which had been brought very much to the fore with regard to the treatment of pulmonary tuberculosis.

Even after this Discussion he had not made up his mind on residential treatment. It had also struck him as curious that no mention had been made of the analogy of leprosy. Lupus was not as rare as leprosy, but it was apparently a rare disease, which made it very difficult to arrange treatment for it and rather difficult to get people interested in it: also there was a social stigma. These were two problems concerning a small section of the population which were of great importance from the humanitarian point of view if no other, and the discussion that afternoon would help towards the solution of one of them.

Dr. F. S. Airey, in replying to Dr. Burrows, said he thought they could obtain from Treloar's and Papworth a good impression of what the tuberculous felt like when segregated. In Stockholm there was a good hostel associated with the Finsen Institute, where patients lived during their stay for short periods of intensive therapy. It was near to the hospital and the men and women were happy and actively employed in general

duties associated with the maintenance of the hostel. It was not State organized, but a philanthropic venture.

The original Finsen lamp was still in use when he was in Stockholm five years ago, and satisfactory results were being obtained. It was the sole form of focal light therapy there employed.

As to the incidence of lupus, he had been about the country during the last ten years and had seen some tragic sights in the remote parts. Statistics were misleading, and so too were the impressions in the minds of many tuberculosis officers. He believed that the actual number of cases in his area was between 300 and 400, and he had made contact with only less than one-half of the afflicted.

Dr. D. E. Macrae, in reply, said that at Treloar's, with about 400 or 500 children in residence, the children affected with lupus were not teased, nor noticed particularly, and therefore were much happier than in ordinary non-institutional life. They lost much of their sense of isolation. He had experience of a colony in which there were 15 or 17 adults, and here again there was no trouble between them.

Dr. A. Burrows, in reply, said that although Kromayer was a good form of treatment, Finsen-Lomholt was quicker, surer and cosmetically more satisfactory.

The diagnosis of lupus vulgaris and its treatment would be more secure if every general practitioner would send to a skin clinic every case of skin disease which had lasted more than three months, but it must be remembered that many patches of lupus were covered by the clothes or looked like nævi to the patient, and were not shown to the doctor, by this means reducing the perfection of any treatment organization. Fear of lupus and its consequences was thus an important factor to be overcome in dealing with the disease by any method which meant public recognition or exposure.

Regarding the prevention of lupus, the notification and proper treatment of such conditions as measles, scarlet fever and whooping cough had reduced its incidence, and no doubt further improvement in food, feeding and economic conditions would help still more.

This was a country which seemed to have a great deal of money waiting to be spent. Let it be spent wisely. Existing institutions should be used for lupus, modifying them as necessary but employing them to the fullest extent possible.

Dr. F. R. G. Heaf, in reply, said that a patient could not be compelled to stay in an institution. There had to be out-patient treatment as well. He put in a plea for provision for the lupus case complicated by lung disease, because it was at the moment an extremely difficult problem to find appropriate treatment. The non-pulmonary diseases hospital did not want such a case because it was infectious, and the pulmonary diseases hospital did not want it because of its non-pulmonary complication. With regard to keeping cases together he would personally deplore a wholly institutional colony entirely for lupus cases. It would be a very trying place from the point of view of securing staff. He would prefer the cases to be spread over the country in special institutions which had accommodation for them.

JOINT DISCUSSION No. 3

Section of Laryngology with Section of Anæsthetics

Chairman—W. M. MOLLISON, M.Ch.

(President of Section of Laryngology)

[*February* 4, 1944]

DISCUSSION ON BRONCHOSCOPY IN THE PREVENTION AND TREATMENT OF TRAUMATIC AND POST-OPERATIVE PULMONARY LESIONS

Lieut.-Colonel Norton Canfield, U.S.A.M.C.: Sometimes when a patient makes unsatisfactory progress or some unusual features develop, the explanation may be a pre-existing foreign body, a benign or malignant growth, or a chronic infectious pneumonitis. Here the bronchoscopist should be able to clear the picture by a single examination. One case was that of a woman who carried a piece of beef bone in her right main bronchus for eleven months, obscured in the X-ray by the heart shadow. Realizing the possibility of a foreign body she was examined and removal of the bone allowed the lung to clear. I once removed some roots of grass from the left main bronchus of a child who injured her chest and was thought to have a resulting empyema. The clearing of the airway was followed by recovery. Unsuspected tumour masses may block a bronchus after injury and a complicated course ensue. Bronchoscopy here is essential and can often settle the diagnosis.

Before operation additional knowledge of the tracheobronchial tree can be obtained by bronchoscopy. With a patient in good surgical condition the procedure is seldom contra-indicated, but following serious or extensive operations, it may be extremely hazardous to subject a patient to the medication and manipulation necessary for broncho-scopy in order to rule out a hitherto unsuspected lesion. Times of operation can be better judged with complete knowledge of the tracheobronchial mucosa as revealed by bronchoscopy.

Post-operative complications.—The dreaded post-operative pneumonia followed by lung abscess has yielded to procedures initiated if not, in fact, actually done by the bronchos-copist. Ever since the recognition that most post-operative lung complications originate from bronchial obstruction, and consequent atelectasis, bronchoscopic methods have played a prominent part in therapy. Many post-operative bronchial obstructions can be relieved by non-bronchoscopic methods. Catheter suction, coughing, breathing of carbon dioxide mixtures and movement of the patient may suffice in most cases, but when these fail, manipulation of the bronchial tree with a rigid instrument and aspiration of secretions have been followed in many cases by proper aeration of the peripheral lung tissue. In my experience these mucus plugs cannot be removed as discrete masses of tenacious mucus because the suction tubes destroy their form when they are aspirated. That they do act as a plug in the bronchi is hardly to be doubted, however, because of the resulting atelectasis and the prompt re-aeration following aspiration. The radiographs do not clear as quickly as the clinical picture probably because of the peribronchial cellular reaction which causes the radio-opacity to persist longer than the bronchial obstruction. Following a long or serious operation the advent of a pulmonary complica-tion may seem to be a contra-indication to further manipulation, but the rapid improve-ment after clearing the airway is ample justification for the procedure. The patient need not be removed from his room or bed. If catheter suction is of no avail bronchoscopic aspiration should be done without the hazard of unduly moving the patient on to an operating table and back to the operating room. With the patient diagonally across the bed and the head in high extended position the aspiration can be easily and expeditiously performed.

One of my most dramatic cases followed a tonsillectomy under local procaine anæs-thesia. The bleeding was slight during the operation and none occurred thereafter. Eight hours following operation the patient was reacting from the narcosis and had difficulty in taking a deep breath. The right chest was dull to percussion and no sputum was being raised. Coughing was encouraged and 5% carbon dioxide in 95% oxygen was used in an attempt to deepen the breathing. As this was unsuccessful broncho-scopic aspiration was performed and prompt aeration of the right lung ensued, with no

further complication. I believe this patient's post-operative narcosis was too deep. It had been induced by phenobarbital-sodium and morphine. The cough reflex was depressed and there was no urge to remove the pulmonary secretions.

The question of narcosis in wartime presents a consideration not usually seen in civilian practice. Men exposed to cold require more morphine for relief of pain. However, when they are evacuated to a warm shelter the drug acts as if it had been stored and becomes available for body distribution. The narcosis thus deepens and the cough reflex is depressed. This series of events is thought by some to favour the advent of atelectasis in wounded men and is undoubtedly a contributing factor in some cases seen in military hospitals.

Post-operative lung abscess.—Believing, as many do, that post-operative lung abscess is a sequel of post-operative atelectasis, I consider that early bronchoscopy is indicated. In patients up to 30 years of age most lung abscesses resolve with rest and postural drainage. Bronchoscopic aspiration is of no assistance in many cases.

During aspiration in cases of lung abscess deep narcosis and general anæsthetics are contra-indicated because coughing during the manipulation is of utmost importance. Only enough analgesic should be used to control the larynx. The abscess is seldom actually reached with the bronchoscope or the aspiration tube, but the sponge-like action of the lungs forces the pus into the bronchus during expiration. If the aspirating tube can then catch the pus before it is sucked back into the abscess much of the actual contents can be removed by repetition of this process. Hence the necessity for maintaining the cough reflex intact. If a series of six or eight aspirations performed about twice a week is not followed by noticeable clinical improvement, this treatment should be discontinued.

Pulmonary medication.—Normal saline is quickly absorbed through the lung. In cases of crusting of tracheal and bronchial tubes in severe acute infection in children, I have often used five to twenty cubic centimetres of saline solution to loosen the crusts with good results.

An injured person may have such pain that bronchoscopy may be inadvisable, but in chest injuries there must be no excuse for leaving the airway blocked by secretion and blood. Medical officers in the African Theatre of Operations have seen many chest injury cases and have used the method of intercostal nerve block to control pain. The injections are made in the paravertebral line just beneath the rib tubercle and include one rib above and one below those involved in the lesion. This allows the patient to cough without pain. If coughing does not remove secretions bronchoscopy can then be used without discomfort. With the clearing of the lungs healing is rapid and pain often does not recur.

Blast injuries of the lung.—In blast injuries to the chest, the patient may not be disabled at once but pulmonary symptoms develop insidiously and he may collapse from respiratory insufficiency. Bleeding from the mouth and nose indicates injury to the respiratory tract and study of these cases has shown the lesions to be in the bronchi and lung tissue. Bronchial obstruction sometimes develops with consequent pulmonary insufficiency. Reports of such cases have come from our colleagues during the air raids in this country and from medical officers in the African and Italian Campaigns. Such cases need attention to the airway when it does not clear spontaneously, to prevent extensive lung damage by supervening infection. Wounds of the chest cause extensive damage which is indicated by expectoration of blood and mucus. After attention to the chest wall the airway may require clearing and again the possibility of bronchoscopic procedures may have therapeutic importance.

So far there has come to our attention very few cases of poison gas casualties, but the pathological lesions are well known. As far as I am aware, no human beings have benefited by tracheobronchial manipulations in cases of irritant gas poisoning. Experimental work on animals has been encouraging, but no work on human beings has been done to my knowledge. The vesicants, however, produce lesions very similar to those found in severe infections of the tracheobronchial mucosa. A necrosing desquamation produces destructive plugs with consequent bronchial occlusion and atelectasis. Removal of these plugs has cleared the airway in patients and arrangements have been made for providing this treatment in gas casualties. Our present methods may need to be improved, but to be aware of the possibilities for removal of the plugs should these cases occur is the responsibility of the bronchoscopist. The chemicals affect the larynx causing ulceration and œdema. This may preclude peroral endoscopy but low tracheo-bronchoscopy through a tracheal stoma may be a life-saving procedure. In such severe lesions as do occur in gas casualties access to the lower trachea and bronchi is much easier with a short endoscope or even certain types of laryngoscope than with the longer tubes used by the peroral route. Tracheobronchial irrigation with saline facilitates the

removal of crusts. Even without endoscopes of any type I believe that the tracheobronchial tree is accessible through a large tracheal stoma. Crusts can be removed with forceps, coughing, and the help of irrigating solutions.

M. D. Nosworthy (*Abstract*): The value of bronchoscopy for the removal of foreign bodies and as part of the treatment of lung abscess is unquestioned; yet, when a patient has aspirated vomit during anæsthesia, early bronchoscopy to save him from developing a lung abscess is seldom put into practice.

Negus, in 1933 [1], pointed out that the laryngeal and cough reflexes, ciliary action, and the presence of mucus in the right quantity and of the right quality were the factors which guarded the entrance and prevented infection from gaining a foothold in the lower respiratory tract. The action of belladonna derivatives, sedative drugs, and anæsthetic agents, and the effects of operation, injury, or accident strain and sometimes overwhelm these natural defences.

Let us consider the causes for the accumulation of secretions in the bronchial tree and the reasons why the patient cannot get rid of them. The depressant effect of anæsthetics on ciliary action and their influence upon the mucus carpeting the bronchial tree is of the first importance. Repeated injections of atropine and mixtures containing belladonna make the secretions viscid, and shallow breathing favours their stagnation. The bronchial secretions will be increased by the spread of infection from the upper respiratory tract or by one originating in the lungs themselves. The folly of operating upon a patient only just recovering from a cold or sore throat is now generally realized. The copious secretions produced by stimulant cough mixtures tend to drown a patient whose cough reflex is ineffective. The inhalation of irritant gases or vapours, or the aspiration of vomit, particularly of a vegetable nature, will have the same effect. The irritant qualities of ether are somewhat offset by its properties of relaxing the bronchial musculature and thinning secretions. Respiratory obstruction or cardiac failure may render the respiratory tract œdematous. There may be a great outpouring of mucus following upon a difficult thyroidectomy and a similar condition after thymectomy in a patient taking prostigmine. Finally, blood may be inhaled after injuries or while a patient is under the influence of an anæsthetic, or it may accumulate as a result of wounds involving the lung.

When the cough and laryngeal reflexes are depressed by the patient's low vitality or by the action of narcotic drugs the respiratory tract is very vulnerable. Not only is there the risk of aspiration of foreign material but also secretions already present may allow organisms to flourish, or may cause bronchial obstruction. This state often follows cerebral operations and even relatively minor injuries in debilitated subjects. Effective methods for the prevention of aspiration, although well known, are too often neglected.

There are many reasons why the cough reflex, although active, may be incapable of clearing the tracheobronchial tree. In the first place, a patient propped upright in bed has to cough sputum uphill all the way and, if the secretions are tenacious or copious, an ill man may well become exhausted before he has effected a clearance. The sputum then falls back and he has to start all over again. After secretions have been in contact with the same area of mucous membrane for any length of time that area becomes insensitive: the urge to cough then disappears but the signs of respiratory obstruction remain. If pain is felt at the site of injury or operation on breathing deeply the patient is naturally disinclined to do this, and he may refuse to cough at all or only makes a half-hearted attempt. This is one of the chief reasons for the relatively high incidence of pulmonary complications in patients with abdominal or thoracic wounds. Pain and paradoxical respiration may make the cough inefficient when the thoracic cage has lost its stability. This occurs with a "stove-in" chest from fractured ribs and is also sometimes seen after thoracoplasty. In like fashion, after certain operations on the larynx or when the recurrent nerves have been damaged during a thyroidectomy, the patient is unable to build up an effective pressure to produce an expulsive cough. In these last conditions a tracheotomy is commonly performed and, although in no way improving the power to cough, it relieves respiratory obstruction and provides a ready means for the aspiration of excess secretions.

Unless removed, retained secretions may kill a patient by asphyxia, or may be responsible for atelectasis, pulmonary suppuration or bronchopneumonia. After operation or injury it is important, at frequent intervals, to make sure that the patient can, and does, take a series of deep breaths and cough. This opens up sticky alveoli and keeps secretions on the move. He must also be encouraged to change the position in which he is lying: if he cannot do this himself, his posture must still be changed; a patient must not be left lying for hours undisturbed. Often a patient who is apparently still unconscious can be roused up to breathe deeply and cough on command. These measures constitute the "stir-up" régime advocated by Waters [2]. An unstable chest-wall must be firmly strapped or fixed by layers of plaster of Paris. Regularly laying the patient down flat

and posturing him first on one side and then on the other is most important because not only does this help the drainage of secretions, but it also assists expectoration. Morphine eases the pain of coughing and is therefore of value; individualized dosage and the stir-up régime offset its depressant action. Inhalations of friar's balsam or a mixture containing potassium iodide help to loosen tenacious secretions. A simple emetic is a very effective method of clearing the bronchial tree of a child. If secretions accumulate in spite of these measures—or straightaway in cases of urgency—aspiration therapy gives very gratifying results and saves the patient much discomfort. This treatment may have to be repeated.

It is now generally accepted that atelectasis is due to bronchial occlusion, the air in the portion of lung so isolated being slowly absorbed—from alveoli filled with oxygen or anæsthetic gases absorption takes places very quickly. Occasionally, bronchoscopy reveals occlusion by pressure from enlarged mediastinal glands, or obstruction by an inhaled tooth or by a tumour filling the bronchial lumen. In the vast majority of cases retained secretion is the cause, prophylactic measures having been neglected or unsuccessful. Sometimes spasm of the bronchial musculature during anæsthesia, by closing down the lumen on a small lump of mucus, may be the determining factor in converting a partial into a complete obstruction. To those unfamiliar with modern views on post-operative pulmonary complications I suggest a study of Brock's [3] classical contribution to the subject and also the other writings to which reference is made. Two clinical types of atelectasis may be recognized; in one the patient is acutely ill, in the other he eats and sleeps well and is not distressed by it. In both traumatic and post-operative cases, re-expansion soon takes place in the latter group with simple postural treatment assisted by hand-clapping over the affected area. A similar response is also shown by the majority of patients in the former group, but not by all. Sepsis in the pleural cavity adversely affects the prognosis, and delays re-expansion. When improvement in the condition of an *ill* patient does not take place quickly more drastic treament is called for, as a safeguard against pulmonary suppuration, bronchopneumonia, or the later development of bronchiectasis. Some advise bronchoscopy on *all* patients as soon as the diagnosis of atelectasis is made. I think that this is wrong and, like the routine use of endotracheal anæsthesia, introduces an unnecessary complication. Aspiration is, however, a valuable procedure, and should be carried out as soon as the indications for it arise which often means late at night. Whether clearance is better effected by bronchoscopic aspiration or by "blind" methods of suction is a matter for discussion.

I have myself followed the practice championed by Waters [4], and first pass a widebored Magill endotracheal tube to permit the free ingress of air while suction is being applied to a catheter introduced through its lumen, in fact, a similar "set-up" to that used for aspiration during, or at the end of, operation. Gillespie [5] reminds us that Kuhn [6] used this method for removing excess secretions as long ago as 1912. Following the Madison practice, I have found that a portable outfit complete with everything required for cocainization, intubation, and suction is a great convenience.[1] Intubation under local anæsthesia is the method of choice. If the exact procedure and the benefit likely to be derived from it are explained to them beforehand most patients willingly co-operate. I formerly gave the patient the original decicain tablet to suck before spraying the nose and throat with 2% butyn or with 10 or 20% cocaine. The present anethaine tablet must not be used in this way or stomatitis will result. Two anethaine tablets dissolved in an ounce of water may be usefully given, however, as a gargle, if the patient is able. The thoroughness with which the topical application must be applied varies with the individual; if cocainization is incomplete for a fit patient gross laryngeal spasm will occur on intubation, resulting in an alarming degree of anoxia.

If the nasal cavity will accommodate a sufficiently large tube I usually perform blind nasal intubation. For a young man who has a full set of teeth and a large muscular tongue this is less uncomfortable than laryngoscopy, although it never fails to surprise me how easy it usually is to expose the glottis of a patient sitting propped up in bed. A lubricated rubber or Coudé catheter is then introduced, and moved up and down inside the endotracheal tube while suction is applied; the possible risk of occluding one of the smaller bronchi, and deflating the area of lung supplied by it, is avoided by taking care not to introduce the catheter too deeply and by keeping it constantly on the move. During this process the patient is postured to help the drainage of secretions and to assist entrance into each main bronchus. Violent coughing usually results and commonly the patient's condition improves dramatically as soon as the secretions have been removed. His colour, pulse, and respirations are better at once and he loses the tight feeling in his chest. Although full re-expansion of an atelectatic lobe is seldom complete immediately a noticeable change *in the character* of the breath sounds can usually be detected.

[1] Supplied by Medical & Industrial Equipment Co. Ltd., 12, New Cavendish Street, London, W.1.

Before certain thoracic operations some make use of a bronchoscope for the introduction of packs or cuff catheters to confine secretions to the diseased area. Others carry out routine bronchoscopic aspiration as a prophylactic measure both before and after all such operations. When suction during anæsthesia is inefficient this is a wise precaution, but I have not made a routine practice of it. A few years ago I had three patients who, after lobectomy for bronchiectasis, developed an atelectasis which necessitated the subsequent removal of the remaining lobe. All three of these patients were ill at the onset, but in those days I did not do any post-operative suction and none of them were bronchoscoped. Obviously the earlier aspiration therapy is performed on such patients, who do not respond to simple measures, the better the prospects, but whether early bronchoscopy is invariably curative, I do not know.

The point I wish to make is that patients with retained secretions or atelectasis should, in my opinion, be treated by anæsthetists. Although they may not be responsible for this occurrence anæsthetists should make themselves responsible for the treatment, at any rate in the first instance. The anæsthetist is usually familiar with the case and precious time may be lost before a bronchoscopist sees the patient. If anæsthetists took over the treatment of these conditions I am sure that surgeons would be delighted. The anæsthetist should make certain that those patients who are likely to develop pulmonary complications carry out proper breathing exercises before operation, and are "stirred up" and postured afterwards. Then the need for aspiration therapy will not arise so often. If the patient's condition is unrelieved by "blind" aspiration he should call the surgeon's attention to the possible value of bronchoscopy.

SUMMARY

Prophylactic measures and simple postural methods of treatment, efficiently carried out, will prevent the development or quickly cure the great majority of traumatic and post-operative pulmonary complications. When aspiration therapy is indicated atraumatic intubation is easier and is within the capabilities of a far greater number of men than is bronchoscopy. A soft endotracheal tube is much less unpleasant for the patient to accommodate than is a rigid bronchoscope; and the patient can adopt different postures and cough on request without risk of trauma when a soft tube is in place. And since "blind" aspiration is successful in so many patients suffering from retained secretions or atelectasis it seems rational to try it first. If no improvement results bronchoscopy should not be long delayed since effective early treatment for these patients is so important. In the first instance there may be just a backwater of watery mucus which moves to and fro on respiration, or an accumulation of thick mucopus or blood. To find a thick gelatinous plug of mucus, of the consistency of glue, is rare in my experience, perhaps because I seldom use atropine or possibly because this is a late phenomenon. Not all post-operative pneumonias originate from untreated atelectasis; a fulminating septic pneumonitis is not a very uncommon complication in those whose health has been undermined by sepsis or cachexia. In such cases even early bronchoscopy will not prevent a fatal outcome and its practice may bring aspiration therapy into disrepute.

REFERENCES
1 NEGUS, V. E. (1933) *Proc. R. Soc. Med.*, 26, 1127.
2 WATERS, RALPH M. (1940) *Anesthesiology*, 1, 136; (1942) Fundamentals of Anesthesia, National Research Council A.M.A., 152.
3 BROCK, R. C. (1936) *Guy's Hosp. Rep.*, 86, 191.
4 WATERS, RALPH M. (1942) *Brit. J. Anaesth.*, 18, 1.
5 GILLESPIE, NOEL A. (1941) Endotracheal Anæsthesia, Madison: Univ. Wisc. Press, 171.
6 KUHN, F. (1912) *Zbl. Chir.*, 39, 73 (Band 1).

T. Holmes Sellors said that in thoracic work there was a widespread interest in the use of the bronchoscope. There were two dominant features in complications in the chest, first, any increase in the normal secretions, and secondly any factor which cut down the normal ejecting mechanism or the cough reflex. If a disease, such as lung abscess or bronchiectasis was considered, it would be found that there were excessive secretions, but that this excess factor was not anything like as important as the mechanism of cough expulsion. Conservatively these cases did not suffer great inconvenience so long as coughing was adequate, and they could be helped to get rid of their secretions by postural drainage. But if anything happened which interfered with the cough reflex (anæsthesia, narcotics and even sleep) there was the potential risk of bronchial "embolism" or bronchogenic spread leading to further pulmonary infection.

Pain and shock were other great factors in cutting down effective coughing. Since the war there had been a number of cases of atelectasis following on direct chest injury or injury elsewhere. The patients were often severely shocked and were suffering great pain; in consequence the cough reflex was depressed or suppressed, and a subsequent patchy or massive collapse was common. The alleged danger of using morphia in too large doses in this type of case was quite unfounded; the benefits derived often enabled

the patient to clear his air-tubes. If these cases could be seen in the early stages all efforts to remove retained secretions should be made, but if these failed bronchoscopic aspiration should be tried. The future of those who develop atelectasis was naturally more hazardous than it would have been if aerated lung could have been guaranteed at the outset.

Unfortunately many cases were not seen early enough, but some which were sucked out after failure of conservative measures had responded very favourably. An interesting and illustrative case was one which resulted from an anæsthetic explosion. The damage to lung was produced by a powerful blast wave down the trachea, which was partially ruptured, and spent its force on the lung tissue. The mechanism was, in other words, that of internally applied blast. He saw this patient about half an hour after the incident and by immediate bronchoscopy removed quantities of blood and mucus with relief of symptoms. The tear in the posterior tracheal wall was also inspected. At a later date a bilateral atelectasis developed which was treated by bronchoscopy in addition to postural drainage and within a few weeks the chest was virtually normal. This case illustrated two phases of bronchoscopic treatment: one, the removal of secretions in the state of severe shock, and the other when massive collapse had started.

When the actual practice of chest surgery is considered the use of the bronchoscope could be discussed in three stages. First, there was the pre-operative phase in which the bronchoscope was really required as an adjunct to postural drainage which was not completely effective. The procedure might have to be carried out at the actual start of the operation if, on anæsthetic induction or on movement, a patient with plenty of sputum suddenly showed signs of respiratory obstruction. In this event suction and clearing of the air-tubes was very important before starting the actual operation. Chest patients were usually lying on the "good" lung, and that was the side that was liable to be flooded. He recalled the case of a young child with extensive bronchiectasis who was thought to have an adherent pleural cavity. However the lung was free and on incision of the pleura the lung collapsed suddenly. This dislodged pus which passed into the opposite side and, even though the bronchoscope was passed within forty-five to sixty seconds, the fluid had gone beyond the range of the suction tube. The child died from drowning.

During operation he did not think that any chest surgeon would work without a bronchoscope at his elbow. Manipulation of lung may extrude pus and secretions into the main bronchi and if these were dispersed into the dependent air-tubes serious respiratory embarrassment would follow. The obstructive signs came on quite silently in many cases and could easily be overlooked. Sometimes the patient's colour appeared good owing to the high concentration of oxygen in the anæsthetic, and, in spite of this, anoxia developed. The only indication of this might be a slowing of the pulse-rate. On occasions the course of an intrathoracic operation had to be interrupted so that the patient could be bronchoscoped to ensure that the bronchi were free from any obstructing material. This can undoubtedly be a life-saving measure, although a disturbance to normal operating technique, and it should only be used if simple blind intratracheal suction failed. Bronchus blocking was commonly used in intrathoracic work to avoid flooding of the "good" lung, but unexpected hæmorrhages or some technical difficulty in blocking did not always obviate the dangers described.

At the end of the operation it was a wise move to make quite sure that the bronchi were free from loose secretions and, if there were any, to remove them by suction. The method was not of much importance so long as the technique was within the capacity of the operator, but the advantage of bronchoscopy was that it could ensure that each of the major air-tubes was clear. It was slightly more satisfactory, though more disturbing, than working blindly with a catheter.

In late complications the value of bronchoscopy was more disputed. In a case of early pulmonary collapse aspiration could be used, but it was of little value after the first few hours had passed because the damage would have been done as the mucus and foreign material had descended beyond the range of the bronchoscope. Cases which were bronchoscoped without delay often recovered dramatically and rapidly, and a fully aerated lung could be anticipated in a high proportion of them.

The more senior members of the team who could use either bronchoscopy or "blind" intubation preferred the former. The junior members were trained to use blind intratracheal methods and with comparatively short practice obtained considerable dexterity. He held that only the minimum of preliminary local anæsthetization was necessary. The use of pentothal in a "wet" case was felt to be dangerous: early relaxation followed by dislodging of secretion led to some obstruction with resultant spasm and it might become impossible to pass the bronchoscope. The development of blind intubation had certainly enlarged the potential field for endobronchial aspiration and the method was one that had considerable advantages when prolonged or continuous suction was likely to be

required. In the absence of a skilled endoscopist who might prefer to use a broncho-scope, the "blind" method did not have the same dangers of bronchial trauma or disturbance to a distressed patient.

V. E. Negus said that he could add his testimony to the evidence which had been given concerning the value of bronchoscopy.

The whole problem was one of bronchial obstruction, whether by foreign body, by growth, or in warfare, by a piece of metal. If for any reason there was blockage of a bronchus, infection would occur with subsequent suppuration. Liquid blood did not do much harm. It had been pointed out by different observers that a certain amount of blood got in in many tonsillectomies, with little harm. But with clots it was a different matter. A clot coming from the tooth or tonsil area was infected, and was more important than liquid blood. Every breath taken must mean that organisms were carried down. Some of them were caught in the nose, but many reached the bronchial tree. Usually they were removed by ciliary action, and this was of great importance. The cilia could not work if the bronchioles were blocked by mucus or a foreign body, nor could they work if the mucus was dried up by excessive amounts of atropin.

R. C. Brock said that it was important to consider how often aspiration of the bronchial tree was really needed. He saw many cases of post-operative chest complications and it was often not a question of deciding between the use of bronchoscopy or aspiration by a catheter but of the complete neglect of the ordinary simple methods of preventing retention of secretion. He was often asked urgently to bronchoscope a patient with atelectasis and audible bubbling of secretion in the trachea, and yet no postural drainage of any sort had been used; as Dr. Nosworthy had already said most clearly the first, second and third line of defence was the routine use of posture and simple methods both to prevent atelectasis occurring, or when it had occurred to get the patient to cough his sputum up by himself. If these simple methods were used the problem of bronchial aspiration would rarely arise. He insisted that all his cases, abdominal and thoracic, were turned flat on their side at least twice a day and urged to cough. Sometimes it might not be possible to do this drill, but when it was done properly and conscientiously, perhaps with the surgeon helping on the first occasion in a difficult case, a great deal of post-operative chest trouble would be prevented.

A number of patients suffered a true pneumonic condition from the start of the post-operative period and it was very difficult at times to decide whether a patient had got simple atelectasis or a condition much more serious. There was a proportion of patients, particularly the debilitated, elderly or very sick, in whom the pulmonary complication was grave from the beginning and was almost certain to prove fatal whatever was done. Inhalation of vomit, for instance, might produce severe irreversible changes in the lung in addition to atelectasis, and aspiration of the bronchi would achieve little. A patient with a severe pneumonia might be made worse by bronchoscopy. He was fully in agreement with the views expressed as to the value of bronchoscopy and of catheter suction in selected cases, but suction was not without danger both during operation and in the post-operative phase. Excessive suction could produce the complete and rapid deflation of a whole lobe or even a whole lung. The over-enthusiastic or over-conscientious anæsthetist could do a great deal of harm in this way.

W. W. Mushin said that the Nuffield Department of Anæsthetics at Oxford kept careful records of all patients during the post-operative period. Atelectasis or collapse of part of the lung was not diagnosed unless there was good clinical evidence and usually good X-ray evidence as well. The examination of the patient and the diagnosis of this condition were made by a senior member of the anæsthetic department, and assistants in that department were taught the methods of examination and diagnosis of these chest conditions. Tracheal suction had been done on a number of these patients, and certain tentative conclusions had been reached about its value.

The great majority of the patients who had atelectasis would get better of their own accord if encouraged to undertake breathing exercises, cough vigorously, move about in bed, and to use posture as an aid to drainage. The more robust the patient the more likely he was to recover with this treatment. A feeble patient or one who was debilitated by his original disease or as the result of a prolonged shock-producing operation was the sort of patient who was likely to get a secondary infection on top of the atelectasis and develop bronchopneumonia. If a patient was of this clinical type, or the involvement of the lung with the collapse was sufficient to cause dyspnœa and a respiratory rate of 30 or 40 or even more a minute, and if he had cyanosis as well as tachycardia and high temperature, trachial suction should be done without hesitation. The majority of these patients showed signs of recovery within the next two to four days.

Another group of patients in whom tracheal suction had proved most beneficial and

the patient to clear his air-tubes. If these cases could be seen in the early stages all efforts to remove retained secretions should be made, but if these failed bronchoscopic aspiration should be tried. The future of those who develop atelectasis was naturally more hazardous than it would have been if aerated lung could have been guaranteed at the outset.

Unfortunately many cases were not seen early enough, but some which were sucked out after failure of conservative measures had responded very favourably. An interesting and illustrative case was one which resulted from an anæsthetic explosion. The damage to lung was produced by a powerful blast wave down the trachea, which was partially ruptured, and spent its force on the lung tissue. The mechanism was, in other words, that of internally applied blast. He saw this patient about half an hour after the incident and by immediate bronchoscopy removed quantities of blood and mucus with relief of symptoms. The tear in the posterior tracheal wall was also inspected. At a later date a bilateral atelectasis developed which was treated by bronchoscopy in addition to postural drainage and within a few weeks the chest was virtually normal. This case illustrated two phases of bronchoscopic treatment: one, the removal of secretions in the state of severe shock, and the other when massive collapse had started.

When the actual practice of chest surgery is considered the use of the bronchoscope could be discussed in three stages. First, there was the pre-operative phase in which the bronchoscope was really required as an adjunct to postural drainage which was not completely effective. The procedure might have to be carried out at the actual start of the operation if, on anæsthetic induction or on movement, a patient with plenty of sputum suddenly showed signs of respiratory obstruction. In this event suction and clearing of the air-tubes was very important before starting the actual operation. Chest patients were usually lying on the "good" lung, and that was the side that was liable to be flooded. He recalled the case of a young child with extensive bronchiectasis who was thought to have an adherent pleural cavity. However the lung was free and on incision of the pleura the lung collapsed suddenly. This dislodged pus which passed into the opposite side and, even though the bronchoscope was passed within forty-five to sixty seconds, the fluid had gone beyond the range of the suction tube. The child died from drowning.

During operation he did not think that any chest surgeon would work without a bronchoscope at his elbow. Manipulation of lung may extrude pus and secretions into the main bronchi and if these were dispersed into the dependent air-tubes serious respiratory embarrassment would follow. The obstructive signs came on quite silently in many cases and could easily be overlooked. Sometimes the patient's colour appeared good owing to the high concentration of oxygen in the anæsthetic, and, in spite of this, anoxia developed. The only indication of this might be a slowing of the pulse-rate. On occasions the course of an intrathoracic operation had to be interrupted so that the patient could be bronchoscoped to ensure that the bronchi were free from any obstructing material. This can undoubtedly be a life-saving measure, although a disturbance to normal operating technique, and it should only be used if simple blind intratracheal suction failed. Bronchus blocking was commonly used in intrathoracic work to avoid flooding of the "good" lung, but unexpected hæmorrhages or some technical difficulty in blocking did not always obviate the dangers described.

At the end of the operation it was a wise move to make quite sure that the bronchi were free from loose secretions and, if there were any, to remove them by suction. The method was not of much importance so long as the technique was within the capacity of the operator, but the advantage of bronchoscopy was that it could ensure that each of the major air-tubes was clear. It was slightly more satisfactory, though more disturbing, than working blindly with a catheter.

In late complications the value of bronchoscopy was more disputed. In a case of early pulmonary collapse aspiration could be used, but it was of little value after the first few hours had passed because the damage would have been done as the mucus and foreign material had descended beyond the range of the bronchoscope. Cases which were bronchoscoped without delay often recovered dramatically and rapidly, and a fully aerated lung could be anticipated in a high proportion of them.

The more senior members of the team who could use either bronchoscopy or "blind" intubation preferred the former. The junior members were trained to use blind intratracheal methods and with comparatively short practice obtained considerable dexterity. He held that only the minimum of preliminary local anæsthetization was necessary. The use of pentothal in a "wet" case was felt to be dangerous: early relaxation followed by dislodging of secretion led to some obstruction with resultant spasm and it might become impossible to pass the bronchoscope. The development of blind intubation had certainly enlarged the potential field for endobronchial aspiration and the method was one that had considerable advantages when prolonged or continuous suction was likely to be

Section for the Study of Disease in Children

President—ERIC CROOK, M.Ch.

[*January* 28, 1944]

PAPERS BY A GROUP OF AMERICAN PÆDIATRICIANS.

Introduced by Brigadier-General PAUL R. HAWLEY, U.S.A.M.C.

The American Approach to Allergy in Childhood

By Lieut.-Colonel HENRY N. PRATT, U.S.A.M.C.

ALLERGY, a term coined by von Pirquet, and meaning specifically "altered reactivity", refers to a broad field of immunology including not only the atopic diseases but also drug idiosyncrasy, serum disease, tuberculous allergy, and a host of other conditioned reactions. Atopy is a term devised by Coca and means specifically "strange disease". In this group of diseases fall asthma, hay fever, eczema, urticaria, and some gastro-intestinal disturbances manifested in childhood. They are characterized by a familial predisposition, a multiplicity of manifestations, a blood eosinophilia, the immediate wheal and flare type of skin response, presence of reagins in the serum, and flaring up of the pathological process by contact with specific excitants, usually proteins.

Many types of therapy have been recommended for these diseases, especially for bronchial asthma. Most of this therapy has been of a non-specific nature, for example, deep X-ray therapy, physiotherapy, psychotherapy, fever treatment, the injection of cortin, lipiodol instillation into the bronchial tree, vitamin-B therapy, vitamin-C therapy, histaminase therapy, sympathectomy. This is only a partial list of those recommended treatments some of which came from Britain, some from America, and others from Canada. No one of these seems to solve the allergic problem, though in individual cases various types of non-specific therapy are unquestionably of value.

The immunological discoveries of Blackley, Noon, and Harley in Britain and Cooke in America, when carried to their logical conclusions, led to a more specific approach to the atopic diseases. In the hands of American clinicians and investigators this method of attack resulted in the most consistently satisfactory therapeutic results. In America both the scratch and intracutaneous skin tests are used, the latter being the more sensitive. In infants and small children suffering from severe atopic dermatitis where little normal skin is available the method of passive transfer of Prausnitz and Kustner is sometimes used as a diagnostic procedure.

In large pædiatric allergy clinics in America the first and most important step is a careful history, taken primarily from the point of view of specific immunological offen-ders. In our clinic at the Boston Children's Hospital we have a four-page form to be used as a guide by the House staff, which is trained in the clinic. Printed forms tend to reduce initiative, therefore every effort is made to individualize the history of the patient. Questions framed to elicit specific sensitivities are suggested. For example: Does the child wheeze more when covered with a feather-stuffed quilt? Is his sneezing and drippy nose increased by sleeping on a kapok-stuffed pillow? Is his eczema or atopic dermatitis exacerbated by eating egg or having contact with some household pet? After the history, comes a painstaking physical examination, especially in relation to growth and development. Vitamin deficiencies and endocrine abnormalities are rarely encoun-tered. Usually a blood study is made primarily to determine the percentage of eosino-phils and the presence of leucocytosis when there is secondary infection. The urine is routinely checked. Approximately 60 scratch tests including the common pollens.

MAY—DIS. IN CHILD. 1

of great immediate relief to the patient himself were those who had a quantity of secretion retained in the trachea or bronchi. These were usually elderly people in poor condition who had had a chronic bronchitis before operation and this had become exacerbated as a result of having an intra-abdominal operation. The vast majority of the tracheal suctions for post-operative complications had been done by lightly cocainizing the pharynx and nose with a spray, and passing a small rubber endotracheal tube blindly through the nose into the trachea. Through this was passed a well-greased gum elastic suction catheter long enough to reach beyond the bifurcation of the trachea. The initial spasm of coughing produced by passing the rubber tube soon ceased and suction could then be done deliberately. Large amounts of secretion were often removed this way, and even those patients with little free secretion seemed to benefit from the procedure. It did not require any premedication and was done in the patient's bed.

There were thus two main types of patient in whom this type of tracheal suction might be done post-operatively: (1) those who, even in the absence of clinical signs of atelectasis, had abundant and obvious secretion in the trachea and bronchi which they could not get up; (2) those who were diagnosed clinically and radiologically as having atelectasis and did not seem to have a sufficiently robust physique to cure themselves by breathing exercises and coughing, and who might otherwise develop bronchopneumonia.

Major R. A. Gordon, R.C.A.M.C., described two cases which represented (1) a type which had not been mentioned in the discussion, and (2) a case of post-operative complication in a patient who had been severely wounded.

The first patient had a severe head injury. Many such patients had a much depressed or absent cough reflex, and they were difficult nursing problems. Frequently these patients filled up with secretion and developed a degree of atelectasis which had to be relieved promptly or else they would die. They did not stand anoxia well, and when the cardiovascular system collapsed, as it did in association with massive atelectasis, unless something was done the case quickly had a fatal termination. This case following head injury developed respiratory distress, with a sudden rise of temperature and was showing signs of cardiovascular collapse. The diagnosis of atelectasis in the left lower lobe was easily made. The routine with these patients had been to suck them out with a catheter. This procedure had been used for two days in the case of that patient. The catheter was again passed, and a considerable amount of secretion was obtained, but there was no change. He was bronchoscoped, and it was found that his left lower main bronchus was completely filled with a frothy white fluid. That was removed by suction, and the patient, immediately on removal of the bronchoscope, was a good colour, his peripheral circulation was rapidly recovering, and his respiratory rate was countable whilst previously he had been gasping. Six hours later the picture recurred. The bronchoscope was passed again with the same result. Aspiration of accumulated secretion was repeated the following morning. In all it was done five times before this patient finally died. The specimen of his trachea, bronchi, and lungs showed no evidence of any trauma or pneumonia.

Mr. Brock had said that it was possible to collapse a lobe of the lung with blind suction. A friend of his presented a case of atelectasis treated by this method, and he had certainly cured the man of atelectasis on the right side. He was hard put to explain why the patient immediately after treatment had a collapse of the left lower lobe, and that was the danger which was liable to be overlooked. Mucous membrane did not stand up well to the frequent repetition of catheter suction. Eventually small areas of hæmorrhage and reactionary œdema occurred, and in the unit in which he was working the sisters did not like to use the suction catheter frequently; they realized the trauma which could be brought about by such means.

With regard to the effects of blast, a patient had been severely wounded in Sicily in his right axilla and groin and came to the hospital for plastic treatment. He developed acute appendicitis, and appendicectomy was performed. Twenty hours later he had a respiratory rate of 33, he was cyanosed, and had a temperature which increased within an hour from normal to 103·8. He had no air entry into the right lower lobe, but no other signs of collapse of the lung. A suction catheter was of little use. Therefore bronchoscopy was done. The right lower lobe bronchus was found to be filled with sticky mucus, which was removed by suction. Respiratory rate came down to 20 immediately. Later radiological study of the chest demonstrated an emphysema of the right lung confined to the lower lobe. On forced expiration this lung failed to collapse, and the mediastinum shifted sharply to the left as the left lung collapsed. On this basis a diagnosis of obstructive emphysema was made. Bronchoscopy and lipiodol bronchograms failed to demonstrate any obstruction, but emphysematous areas were filled by the lipiodol. There was still *no satisfactory reason for the failure of the lung to collapse,* except the possibility of a blast effect, since the man was wounded by H.E. shell.

(1) Primary, in which there is systemic as well as variable local involvement and no history of previous stomatitis or labial herpes. (2) Recurrent, in which there is variable local but no systemic involvement, and usually a previous history of stomatitis or labial herpes and is in fact an equivalent of recurrent labial herpes.

Complications consist of: (1) Dehydration brought on by refusal of food and fluids by mouth. (2) Impetiginization of accompanying labial herpes. (3) Paronychia in thumb suckers.

The herpetic ætiology of this condition is shown: (*a*) By demonstrating the virus of herpes in the saliva or from the lesions; (*b*) by demonstrating the development of antibodies against a known herpes virus during the course of an attack. (*a*) The saliva or a swab from a mouth lesion is rubbed on to the scarified cornea of a rabbit. In thirty-six to seventy-two hours as a rule a well-marked kerato-conjunctivitis develops. Sections of the cornea show the presence of eosinophilic intranuclear inclusion bodies characteristic of herpes simplex. If at the same time the nictitating membrane is removed, washed in sterile saline, ground and injected into the brains of two sets of mice, one set normal and one set immune to the herpes virus, the former will develop encephalitis in three to ten days, while the latter will remain well.

(*b*) Blood taken from the patient early in the disease will not protect mice from infection with a known herpes virus while that taken after recovery from the illness will. Black inoculated the gently scarified gums of a 12-month old child with the contents of a herpetic vesicle. On the third day the child began an illness typical of that described above. He was able to isolate the virus from her mouth and to demonstrate in her blood the development of antibodies against the herpes virus.

Certain epidemiological data have been accumulated: (1) The incubation period may be as short as three days. (2) Newborn babies are, as a rule, immune to infection because of the presence of maternal antibodies in their circulation, since most adults have immune bodies in the blood; by analogy with measles and other virus disease, this immunity probably disappears about the age of 6 to 12 months. At this time teeth are being cut but it seems probable that the absence of antibodies is more important in pathogenesis than the presence of teeth which has been stressed heretofore. (3) The disease can occur in epidemics and several family epidemics have been described. Since the probable source of infection is the saliva of adults either intermittent or chronic carriers, or an outspoken labial herpes, and since the youngest child tends to be cuddled and kissed more than the older children, it is this child that frequently is the first victim, the disease then spreading to the next oldest, and so on.

There are many phases of the disease to be investigated, among others the reason for the *preponderance of cases in late autumn and early spring*; this might very well be done in the various nurseries established for the under-5-year-olds, where epidemics do occur.

Treatment is entirely palliative and consists of preventing dehydration, by parenteral fluids if necessary, remembering that cold fluids by mouth are more acceptable than warm; the local application of chromic acid or gentian violet to the mouth lesions to alleviate pain; maintaining mouth cleanliness; treating secondary infection and reassuring the anxious mother.

REFERENCES

BLACK, W. C. (1938) *Amer. J. Dis. Child.*, 56, 126.
—— (1942) *J. Pediat.*, 20, 145.
BURNET, F. M., and WILLIAMS, S. W. (1939) *Med. J. Aust.*, 1, 637.
DODD, KATHERINE, BUDDINGH, JOHN, and JOHNSTON, LELAND (1939) *Amer. J. Dis. Child.*, 58, 907.
SCOTT, T. F. McNAIR, and STEIGMAN, ALEX J. (1941) *J. Amer. Med. Ass.*, 117, 999.

Fibrosis of the Pancreas in Infants and Children

Major C. D. MAY, U.S.A.M.C.

IN fibrosis of the pancreas almost all the exocrine portion of the gland is profoundly affected. The acini and small ducts are greatly dilated by an inspissated secretion. Frequently the lumina of the ducts and acini are so markedly dilated that the appearance is that of a "cystic" structure but there are no true cysts. Extensive fibrosis is found. The islets of Langerhans are not involved; they appear and function quite normally. On the other hand the damage to the acini is so severe and widespread that normal production of enzymes by the pancreas is inconceivable.

moulds, dusts, animal epithelia, and foods are made. If one or more satisfactory reactions are observed and if the reactions indicate sensitivities consistent with the history, no further testing is done. If no reactions occur, intracutaneous tests are applied, usually 16 at each of two or more sittings. Following this, the interesting part of the study takes place. This consists of a correlation of the history with skin reactions. All suspected offenders are abolished from the child's environment or diet, and he is desensitized to those substances such as pollens and house dust which he cannot avoid. During his weekly clinic visits in subsequent months clinical trial of the various specific offenders is made. For example: If it is suspected that the child is sensitive to cottonseed, he will be permitted to sleep on a cotton-stuffed pillow for one night or until symptoms occur.

The ever-increasing size of pædiatric allergy clinics clearly indicates the relatively satisfactory results which are obtained by this tedious method.

Whereas British pædiatricians and allergists not infrequently attempt desensitization with mixtures of dusts, pollens, and animal epithelia, in America a greater effort at specificity is made.

The fundamental factor which makes one person respond violently to a substance which is innocuous to most is not known. A long chain of circumstances result in the allergic explosion. The only link in this chain which has yet been broken is the immunological one, which, at the moment, seems the best method of attack. No matter how much physiotherapy or psychotherapy is given to an individual child suffering from asthma, he will continue to wheeze so long as the household cat, to which he is sensitive, remains a pet.

I do not believe the immunological approach is the ultimate solution to the atopic diseases. The most rational approach is through the autonomic nervous system, especially in relation to the parasympathetic nerve endings, the secretion of acetylcholine, and the physiology of histamine or some similar substance such as Lewis's H-substance, which activates the fundamental physiological response of increased capillary permeability, smooth muscle spasm, and eosinophilic infiltration, which are the fundamental responses in the allergic reaction. For this reason much can be said for the methods other than immunological which are more prevalent in Britain than in America.

Herpetic Stomatitis in Infants and Children

By Major T. F. McNair Scott, U.S.A.M.C.

Apart from affections of the mouth associated with avitaminosis, blood dyscrasias, specific bacterial or fungus infections, there is a common stomatitis occurring among infants and young children that has been called by many names, such as aphthous, membranous, ulcerative or Vincent's stomatitis. The evidence to be presented is sufficiently conclusive to show that these types of stomatitis are really one disease, with a clinical picture varying somewhat with the severity, due to a primary infection with the virus of herpes simplex and hence can all be called herpetic stomatitis.

Black (1938) considered all these varieties to be a clinical entity possibly caused by a virus. Dodd *et al.* (1939) demonstrated the presence of herpes virus in the saliva of children suffering from this disease. Burnet and Williams (1939) not only demonstrated the virus but also showed that following an attack of this stomatitis, children developed antibodies against a known herpes virus. Scott and Steigman (1941) in Philadelphia and Black (1942) in California, working independently, confirmed these findings.

The clinical picture of the disease is as follows: It attacks children between the ages of 1 and 6 years as a rule; the onset is sudden with fever, which may be as high as 105° F., irritability, anorexia and malaise, which symptoms may coincide with the onset of a sore mouth or may precede this by several days. The disease usually lasts seven to fourteen days, the symptoms of pain and fever tending to subside before the disappearance of the visible signs in the mucous membranes. The objective local findings are: (1) Changes in the gums which vary from a thin hyperæmic line along the dental margins to a considerable degree of redness and spongy swelling. (2) Shallow yellowish painful ulcers on the tongue and buccal mucous membranes, the result of ruptured vesicles which can be seen as such very early in the disease; occasionally the tonsils and pharynx are affected early, leading to a misdiagnosis of follicular tonsillitis. (3) Enlargement of the regional lymph nodes, which may persist for several weeks after the acute phase is over. (4) Marked oral fœtor. There are two main types of the disease:

(1) Primary, in which there is systemic as well as variable local involvement and no history of previous stomatitis or labial herpes. (2) Recurrent, in which there is variable local but no systemic involvement, and usually a previous history of stomatitis or labial herpes and is in fact an equivalent of recurrent labial herpes.

Complications consist of: (1) Dehydration brought on by refusal of food and fluids by mouth. (2) Impetiginization of accompanying labial herpes. (3) Paronychia in thumb suckers.

The herpetic ætiology of this condition is shown: (a) By demonstrating the virus of herpes in the saliva or from the lesions; (b) by demonstrating the development of antibodies against a known herpes virus during the course of an attack. (a) The saliva or a swab from a mouth lesion is rubbed on to the scarified cornea of a rabbit. In thirty-six to seventy-two hours as a rule a well-marked kerato-conjunctivitis develops. Sections of the cornea show the presence of eosinophilic intranuclear inclusion bodies characteristic of herpes simplex. If at the same time the nictitating membrane is removed, washed in sterile saline, ground and injected into the brains of two sets of mice, one set normal and one set immune to the herpes virus, the former will develop encephalitis in three to ten days, while the latter will remain well.

(b) Blood taken from the patient early in the disease will not protect mice from infection with a known herpes virus while that taken after recovery from the illness will. Black inoculated the gently scarified gums of a 12-month old child with the contents of a herpetic vesicle. On the third day the child began an illness typical of that described above. He was able to isolate the virus from her mouth and to demonstrate in her blood the development of antibodies against the herpes virus.

Certain epidemiological data have been accumulated: (1) The incubation period may be as short as three days. (2) Newborn babies are, as a rule, immune to infection because of the presence of maternal antibodies in their circulation, since most adults have immune bodies in the blood; by analogy with measles and other virus disease, this immunity probably disappears about the age of 6 to 12 months. At this time teeth are being cut but it seems probable that the absence of antibodies is more important in pathogenesis than the presence of teeth which has been stressed heretofore. (3) The disease can occur in epidemics and several family epidemics have been described. Since the probable source of infection is the saliva of adults either intermittent or chronic carriers, or an outspoken labial herpes, and since the youngest child tends to be cuddled and kissed more than the older children, it is this child that frequently is the first victim, the disease then spreading to the next oldest, and so on.

There are many phases of the disease to be investigated, among others the reason for the preponderance of cases in late autumn and early spring; this might very well be done in the various nurseries established for the under-5-year-olds, where epidemics do occur.

Treatment is entirely palliative and consists of preventing dehydration, by parenteral fluids if necessary, remembering that cold fluids by mouth are more acceptable than warm; the local application of chromic acid or gentian violet to the mouth lesions to alleviate pain; maintaining mouth cleanliness; treating secondary infection and reassuring the anxious mother.

REFERENCES

BLACK, W. C. (1938) *Amer. J. Dis. Child.*, 56, 126.
—— (1942) *J. Pediat.*, 20, 145.
BURNET, F. M., and WILLIAMS, S. W. (1939) *Med. J. Aust.*, 1, 637.
DODD, KATHERINE, BUDDINGH, JOHN, and JOHNSTON, LELAND (1939) *Amer. J. Dis. Child.*, 58, 907.
SCOTT, T. F. McNAIR, and STEIGMAN, ALEX J. (1941) *J. Amer. Med. Ass.*, 117, 999.

Fibrosis of the Pancreas in Infants and Children

Major C. D. MAY, U.S.A.M.C.

In fibrosis of the pancreas almost all the exocrine portion of the gland is profoundly affected. The acini and small ducts are greatly dilated by an inspissated secretion. Frequently the lumina of the ducts and acini are so markedly dilated that the appearance is that of a "cystic" structure but there are no true cysts. Extensive fibrosis is found. The islets of Langerhans are not involved: they appear and function quite normally. On the other hand the damage to the acini is so severe and widespread that normal production of enzymes by the pancreas is inconceivable.

This lesion in the pancreas has been found at necropsies of infants and isolated reports have appeared in the literature for many years. However, association with the symptoms during life was inadequate and its frequency was unsuspected, because routine microscopic examination of the pancreas had been neglected.

During fifteen years at the infants' and children's hospitals in Boston 35 examples of this lesion were encountered in examinations of the pancreas in 2,800 necropsies. Since a communication reporting these (Blackfan and May; 1938) about 25 additional examples of the disease have been encountered. In the same year two other papers (Harper, 1938; Andersen, 1938) from clinics where the pancreas was examined miscroscopically at necropsy presented similar series of patients. In these and subsequent reports the incidence of the disease has been found to be 1% to 3% of all patients autopsied.

Our experience with approximately 60 patients with this lesion in the pancreas has enabled us to become reasonably accurate in diagnosis during life and to provide some suggestions for treatment.

Clinical symptoms (four groups).—Group 1: Dying within a few days of birth, usually as the result of intestinal obstruction by an inspissated meconium.

Group 2: The majority of patients having this lesion in the pancreas develop symptoms referable either to the gastro-intestinal system or to the respiratory system and frequently both systems are disturbed. Failure to gain in weight in spite of an adequate food intake and a good appetite is usual. A cough and signs of pulmonary infiltration ultimately appear. Diarrhœa or altered stools are a regular feature. When the patients are ill a relatively short time (eight months) before death the features are indistinguishable from many disorders causing chronic wasting and terminal bronchopneumonia.

Group 3: If the illness lasts longer (sixteen months) the clinical appearance is likely to be dominated by the development of large pale offensive "fatty" stools, abdominal distension, and extreme emaciation. In fact the appearance is similar to that seen in cœliac disease except that by this time the pulmonary involvement is usually conspicuous and gives a clue to the real basis of the symptoms. ·

Group 4: Symptoms appear at or soon after birth in the great majority of·patients. Rarely two to four years may pass without any disorder attracting attention, and the child may appear healthy and well nourished. Close inquiry will reveal that from an early age stools have been abnormal, the appetite extraordinarily good, and a chronic cough had developed. No child with this lesion in the pancreas has been reported to have lived longer than 15 years.

An additional feature is that more than one sibling in a family is often affected. The pneumonia is an interstitial bronchopneumonia with destruction of bronchial walls leading to bronchiectasis with abscesses and fibrosis.

Consequences of this lesion in the pancreas.—(1) Marked impairment of digestion of food due to almost complete lack of trypsin, lipase and amylase from the pancreas. This defect persists throughout the life of the patient, no improvement having been noted to occur by direct estimation of the enzymes even when the nutritional state is restored to normal. (2) Bulk of fæces increased. (3) Fat content of fæces increased but the fat is usually present in split forms as in the normal person, i.e. the neutral fat is not increased. (4) Nitrogen (from undigested proteins) in fæces is increased. (5) Curve of blood sugars in glucose tolerance test is often flat but may be normal (about 25%), and is never of the diabetic type. (6) Absorption of fat-soluble vitamins A, D, and K, is impaired but not completely defective.

Diagnosis.—The characteristic history and clinical symptoms may *suggest* the diagnosis but it can only be *established* by estimation of the concentration of pancreatic enzymes in the duodenum. The pancreatic juice is easily obtained by passing a tube into the duodenum. Trypsin is most easily and accurately determined and suffices for ordinary clinical purposes (Andersen and Early, 1942).

In the differential diagnosis cœliac disease presents the greatest difficulty; the following table may be of aid:

	Fibrosis of pancreas	Cœliac disease
Onset	Birth	9 months
Familial	Commonly	Rarely
Appetite	Good	Poor
Pulmonary infection	Present	Absent
Pancreatic enzymes	Absent	Normal
Nitrogen in fæces	Increased	Normal
Glucose tolerance curve	Flat or normal	Flat
Wasting	+	+
Abdominal distension	+	+
Fatty stools	+	+
Per cent. fat in fæces	Increased	Increased
Split fat in fæces	Normal	Normal
Clumping in gastro-intestinal rœntgenogram	Present	Present

Treatment.—Based on these considerations: (1) In depancreatized animals amount of food absorbed increases with increased intake. Appetite usually becomes enormous. (2) "Substitution" therapy with enzyme preparations. (3) Use of "predigested" foods. (4) Treatment of pulmonary infection.

Thus when no special therapy is available allow the patient an abundance of all types of food to satisfy the appetite regardless of the appearance of the stools. Fats might be somewhat restricted but not if it makes the diet unattractive.

Use of pancreatin preparations is difficult. Their potency is variable and uncertain. The enzymes are inactivated by the acid of the stomach. Enteric coatings may be removed too soon or too late and the enzymes thereby be ineffective. The daily doses required are large (0 to 4 months—6 g.; 5 years—21 g.). Enteric coated tablets or capsules cannot safely be given to infants when proper treatment is most urgent. Granules, individually enteric coated, may be practical for infants.

Predigested foods offer great promise for treatment during infancy and early childhood. Hydrolysates of casein[1] are now available on a commercial scale. These hydrolysates are biologically equivalent to the whole protein but are composed primarily of amino-acids. They can therefore be absorbed without digestion and have been utilized to maintain nitrogen balance and a proper nutrition. They can be combined with sugar not requiring digestion like glucose and a minimum of fat and the proper salts and vitamins. Babies have been successfully reared on such mixtures. Their use in treatment of fibrosis of the pancreas has been under trial by us. In a few instances the results are greatly encouraging, in one instance successful. The problem has usually been to restore the nutritional state in the presence of the pulmonary infection. If the diagnosis is not made early and the treatment prompt and efficacious the pulmonary infection is so far advanced as to be irreversible. With increasing acuteness in recognizing the disease the more prompt institution of therapy will undoubtedly improve the results.

The vitamins may be given by mouth but should be administered in doses four times the daily requirements to make up for the impairment in absorption. Addition of the vitamin-B complex to the usual vitamins A, D, and C is desirable.

Treatment of the pulmonary lesion has been unsatisfactory. *Staphylococcus aureus* is almost invariably the sole organism cultured from the bronchiectatic abscesses. This type of infection has not improved with sulphonamide therapy. The improvement of nutrition has been the only hope of controlling the pulmonary lesion. Perhaps penicillin will afford a more successful approach. Ultimate recovery of these patients will depend on recovery from or prevention of the pulmonary infection.

REFERENCES

ANDERSEN, D. (1938) *Amer. J. Dis. Child.*, 56, 344.
—— and EARLY, M. (1942) *Amer. J. Dis. Child.*, 63, 891.
BLACKFAN, K. D., and MAY, C. D. (1938) *J. Pediat.*, 13, 627.
HARPER, M. (1938) *Arch. Dis. Child.*, 56, 45.

A Nutritional Survey of School Children in Oxfordshire, London, and Birmingham

By Captain MILA I. PIERCE, U.S.A.M.C.

THIS report is concerned with a survey of school children, age 5 to 14 years, from several towns and villages of Oxfordshire, Walthamstow, Greater London, and Birmingham between May 17 and July 16, 1943. A total of 681 children were examined. The object of the survey was (1) to compare the physical and nutritional status of children in these various districts; (2) to evaluate the benefits of the school meal.

The survey was conducted by members of the staff of the Oxford Nutrition Survey, Oxford, and was accomplished by a mobile team of four, a pædiatrician, a nutritionist, a nurse, and a technician. The examinations were done in the schools; blood samples were drawn by finger stab and transported to the staff laboratory and prepared for the necessary determinations on the same day.

Particular search was made by physical examination for signs of nutritional defects—i.e. disorders of the skin, mucous surfaces, bony structure and teeth, as well as for signs of chronic ill-health. Blood samples were analysed for (1) the ascorbic acid content by

the method of Mindlin and Butler, for (2) serum proteins by the method of Linderstrom and Lang, and for (3) hæmoglobin by the Haldane method according to the standard technique outlined by the Medical Research Council. A rough estimate of the food habits was obtained by questioning the older children on their diets for the past twenty-four hours, at the time of the examination, and a more detailed inquiry was made by the nutritionist who visited the homes of a limited number.

The children selected for the survey represented a random sample of the school population as far as possible. Selection was restricted to obtain comparable figures as to age, sex and the groups who took and who did not take the school meal.

Schools Selected for the Survey

In Oxfordshire five Town Council Schools with a school population of 200 to 300 each, and four small village schools of 30 to 60 children each were visited, two suburban centres immediately adjacent to Oxford and three towns for the surrounding rural district. Menus were planned by the school dietitian and prepared by a local cook; meat or a meat substitute, potatoes and a sweet were provided daily; a second vegetable was usually, but not always, served.

In Birmingham, two city schools in the heart of the industrial area were visited; school meals were served only to a limited number, as facilities were crowded; no attempt was made to select children in regard to the meal in this area.

In London the three schools visited were in Walthamstow, an industrial centre of Greater London. One school represented the more privileged section of the community; the two other schools were in the crowded sections of the suburb where the standard of living was lower, and the school buildings cramped and dark. In the whole London area food was prepared in a central kitchen and transported to the schools in aluminium containers ready for service: the menus consisted of meat, vegetables, potatoes and a dessert.

Findings of the Survey

(1) *Health ratings.*—Analysis of the physical condition of the children was simplified by grouping the children into two lots, Class A and Class B—the criteria of classification for which were as follows: (1) Body build; (2) posture; (3) weight and subcutaneous fat; (4) skin elasticity and muscle tone; (5) skin colour; (6) facial expression and general habitus; (7) the presence or absence of multiple physical defects, or other signs of ill-health. The Class A group included the children who were healthy, both those who were robust and of normal weight, and those who were thin, but otherwise well. The Class B group included those who were thin and tired or asthenic, and those showing obvious signs of ill-health.

Comparison of the physical rating of children in the four districts revealed that 71·35% of the children in the Oxfordshire towns, 59·33% in the Oxfordshire villages, 63·19% in London, and 43·52% in Birmingham rated as Class A. The percentage rating as Class B was, therefore, 28·64% in Oxfordshire town schools, 40·67% in the Oxfordshire villages, 36·91% in London and 56·48% in the Birmingham schools.

(2) *Physical defects.*—The most common physical defects were skeletal and postural. The incidence of winged scapula, round shoulders, and chest wall deformities was lowest in the Oxfordshire town schools, about 1½ times higher in the village schools, twice as high in London, and more than twice as high in Birmingham. Skin diseases were next most common; the incidence of follicular keratosis ranged from 11 to 15% in all these areas except among the village schoolgirls where it was as high as 33%; the incidence of xerosis ranged from 11 to 21% in all areas, except the villages where it was 21%. The incidence of skin sepsis was low, ranging from 3 to 7% in all areas except Birmingham, where 9·4% of the boys had skin infection. The incidence of scabies ranged from 3 to 6%, except among the village boys, where the incidence was 21·9%. The incidence of gingivitis ranged from 4 to 15% and was most commonly seen in the village children; dental caries was more common to this group. Angular stomatitis and rhagades were seen in 3 to 10% of children in all districts except Birmingham where the incidence among the boys was 12%.

Upper respiratory infections were more common in the village and Birmingham groups, where the incidence was 7-9%, than in either the Oxfordshire towns or London schools where the incidence was 14-18%. The incidence of organic cardiac defects ranged from 1 to 2·7% in all districts.

Blood ascorbic acid findings.—The average level for serum ascorbic acid was 0·30 mg.% for 322 Oxfordshire town children, 0·89 mg.% for 59 village children, 0·49 mg.% for

127 London children and 0·43 mg.% for 96 Birmingham children. In the Oxfordshire group significant differences relative to age were not found; in both the London and the Birmingham groups the values were higher for the ages 7 to 11 years than for the 5 to 7 and 11 to 13 year old children. The average levels for the Class A children were higher than for the Class B children.

Serum protein findings.—The average serum protein levels for 330 children from the Oxfordshire town schools was 6·57 g. per 100 ml., for 58 village children 6·56 g., for 106 Birmingham children 6·71 g., and for 127 London children 6·66 g. There was some variation in the levels of the different age-groups. The average levels for children aged 5 to 7 from all the districts was 6·49 g., for the 7 to 11 year olds 6·63 g., and for the 11 to 13 year olds 6·70 g. The average level for the total of 621 children of all ages was 6·62 g. per 100 ml. This average corresponds to the adult average level for 731 adults examined in Oxford in 1943 by members of the same staff. Levels for girls were 0·13 g. higher than the average level for boys.

Hæmoglobin findings.—The percentage of children with hæmoglobin levels between 81 and 100% (Haldane) in Oxfordshire Town schools was 95·3%, in the Rural schools 95%, in London 91·2%, and in Birmingham 92·1%. These figures compare favourably with those obtained in previous surveys by Davidson (1935) in Aberdeen who found that 100% of the school children had levels above 81% (Haldane), and by Mackay (1942), who found that 68% of the London school children were above 81% (Haldane). Davidson's figures for Edinburgh children in 1943 were lower; 62·7% of the children gave levels of 81% (Haldane).

Findings relative to the school meal.—These findings relate to 231 children who took the school meals and 283 who did not, in schools of Oxfordshire and London in which the meal was made available to the entire school population. In the other districts, either the meal was not served at all, or was restricted to a selected few.

Health ratings.—The distribution of health ratings A and B did not differ strikingly in the group of children who took the school meal from that of the group which did not.

	Number examined				Number	Class A		Class B	
						No.	%	No.	%
Oxfordshire 370		Took school meal.	...	...	164	126	76·8	38	23·2
		Did not take meal	...	...	206	138	67·0	68	33·0
London	144	Took school meal	...	...	67	40	59·7	27	40·3
		Did not take meal	...	...	77	51	66·24	26	33·76

Use of the school meal by children in each health group.—A higher proportion of Class B children were using the school meal in London than in Oxfordshire.

						Number	% taking school meal		% not taking school meal	
Oxfordshire	Class A...	...	...	...	...	264	(126)	47·73	(138)	52·27
	Class B...	...	...	...	...	106	(38)	35·85	(68)	64·15
London	Class A...	...	...	...	...	91	(40)	43·96	(51)	56·04
	Class B...	...	...	...	...	53	(27)	50·94	(26)	49·06

Serum Ascorbic Acid Levels in the Two Groups

The average levels of serum ascorbic acid were not significantly different for the two groups in Oxfordshire, although small differences did occur in favour of the group who did not take the school meal. The same difference was more significant in the London group, where the differences ranged from 0·14 to 0·28 mg.% in the various age-groups, in favour of those not taking the meal.

Serum protein levels.—There was no significant difference in the average serum protein levels for the two groups in the Oxfordshire area, but in the London area differences ranged from 0·20 g. to 0·26 g. in favour of children not taking the school meal. These differences were more apparent in the 11 to 13 year old age-group.

Hæmoglobin levels.—No significant differences were found in the two groups.

Home visits: Interpretation of these findings necessarily must depend upon the analysis of other factors such as the home conditions and diet of the two groups. These factors were considered among 121 children whose homes were visited. The family size of children who took the meal was larger than that of the group not taking the meal. The chief difference in the home diets were the menus for the evening meal: the children who took the school meal more often were served bread, cake and tea, and the group who took the home noon meal were more often served a more substantial tea or supper. It appeared that the family depended upon the school dinner as the main meal of

the day, and indicated' that the family food habits were better among children whose families did not avail themselves of the school meal.

SUMMARY

(1) The general health rating of the children was best in the Oxfordshire town schools. The London schools rated second, the villages third, while the Birmingham school group rated lowest.

(2) Ascorbic acid levels were well below the accepted optimum level in the Oxfordshire town, Birmingham and London schools and within normal range only in the villages. The availability of new potatoes and garden stuffs accounted primarily for the differences.

(3) Indication was found that a correlation exists between blood ascorbic acid levels, within a given group, and the general health of that group.

(4) The school meal, as served in the schools visited, did not raise the blood ascorbic acid levels to that of the group which did not take the meal. Interpretation of the finding necessitates knowledge of the home conditions of the two groups, and also more information regarding the vitamin content of the food as served in the schools. The use of foodstuffs of high vitamin-C content is to be encouraged both for the school and home menus.

(5) The serum protein levels were lowest in the age-group 5 to 7 and highest in the age-group 11 to 13 years. Small but insignificant differences were noted in favour of the group not taking the school meal. No evidence of protein deficiency was found.

(6) Hæmoglobin levels were higher for the school children of all three districts than were recently reported for London and Edinburgh.

(7) Physical examinations gave a more accurate measure of the health status of the children than did the laboratory methods employed in this survey. In districts where the school meal must necessarily be limited, selection by physical rather than by an economic standard seems desirable.

REFERENCES

DAVIDSON, L. S. P., and CAMPELL, R. M. (1935) *Brit. med. J.* (ii), 195.
—— *et al.* (1943) *Brit. med. J.* (ii), 95.
MACKAY, H. M. M. *et al.* (1942) *Lancet* (ii), 32.

Section of Psychiatry

President—W. Norwood East, M.D., F.R.C.P.

[*February* 15, 1944]

Cerebral Dysrhythmia: Its Significance in Aggressive Behaviour

By Denis Hill, M.B., M.R.C.P., D.P.M.

As far as history records there have always been individuals born to lives of emotional maladjustment, perverse sexuality or uncontrolled aggressiveness. At the end of what may be called the anecdotal period of psychiatry, Maudsley expressed the view that sudden violent crimes committed in "blind fury" were frequently due to an epileptic process and he also made the observation that this tendency ran in families. He observed that such persons were frequently the siblings or children of epileptics and he believed that "the impulse sprang from a morbid condition of nerve element". Bleuler, like many other authorities, described a group of psychopathic personalities with abnormal irritability, the brief description of which has not, I think, been bettered. He says: "The irritable types react to influences from without in a very acute and exaggerated manner, which takes the form of attacks of rage lasting mostly a few hours, despair with suicide, anxiety attacks, or stuporose states. During the attack, reflection is altogether inadequate. Some cases are practically in a twilight state; the memory is later markedly clouded; jealousy and alcohol are especially frequent causes for the precipitation." Bleuler's view of these attacks suggests that a clouding of consciousness can occur. In the classification of many authors the term "epileptoid" has been applied to these personalities. Despite the failure of most workers to demonstrate a constant type of personality change among epileptics, this term has been applied to such patients because of their egocentricity, their insensitiveness, and the sudden violence and uncontrolled fury which they exhibit and which is frequently followed by partial or complete amnesia.

The classification which has been used as a basis for all our work at Sutton has been that of D. K. Henderson (1939). In this, psychopaths are divided into predominantly aggressive, predominantly inadequate, and predominantly creative. The numbers of the last mentioned whom we have seen have been so small that nothing can be said regarding them. In a previous contribution which D. J. Watterson and I read to this Section in 1942, we described the electroencephalogram (E.E.G.) findings in Henderson's first two groups, namely, the predominantly aggressive and the predominantly inadequate. In the latter group the finding of 32% E.E.G. abnormality although twice the percentage among controls, was not much higher than among a group of mixed psychoneurotics.

I shall deal only with the predominantly aggressive group of psychopaths among 65% of whom E.E.G. abnormality was found. For the purposes of this paper, I shall call them cases of dysrhythmic aggressive behaviour and for short, cases of D.A.B. In Henderson's classification the aggressive group is subdivided into those who injure others, those who attempt self-injury, alcoholic and drug addicts, the epileptoid and the sex variants. In 1941 we had not made this subdivision into the smaller groups and the cases of sexual perversion were divided between the aggressive and inadequate

groups. As a result of more extended investigations on over 400 psychopaths, it can now be said that in the absence of violent temper, overt aggressiveness or a recurrent tendency to suicide, E.E.G. abnormality is not found in greater incidence in the alcohol or drug addicts or patients with sex perversion, than among psychoneurotics. We are therefore left with those psychopaths whose histories show repeated hostile acts against individuals, a tendency to self-injury, or suicide, and the epileptoid. These predominant characters must in all cases be fitted into an antisocial personality, and not be the transient, even if repeated, expression of a paranoid, schizophrenic, or manic-depressive psychosis.

The clinical material which provides the factual basis of this paper is provided by a total of over 400 psychopathic patients, from whom special groups have been selected for particular purposes.

THE DEVELOPMENT OF THE PSYCHOPATH

The development of neurone structure and the integration of complex patterns in the brain, upon which consciousness and the substratum of personality are built, is a prolonged process which is continued after birth, through infancy and childhood up to the early years of adolescence. Thus myelinization in the fibres of the three large association areas is not complete before the age of 18, and there is considerable individual variation in this respect. Structural development is the precursor of functional organization, and at the present time the best physical indication of the functional organization in the brain is the E.E.G. The increasing organization associated with the appearance of consciousness, the development of mental processes, and the later emergence of personality, are faithfully mirrored in the changing frequencies of the cortical rhythms. As Gibbs, F. A., and Gibbs, E. L. (1941) have written: "The aspect of the electrical activity of the cortex, which correlates best with changes in central nervous function, is its frequency." After birth, when there is very little rhythmic activity, slow frequencies first develop and spread over the brain. These are progressively replaced by faster frequencies until at the age of 9 to 12 many children have normal E.E.G.s. At this age there is a uniformity in the E.E.G.s of normal children. Yet development is by no means complete, for the characters continue to change in many cases until the age of 18. It would appear that between 12 and 18, the E.E.G. acquires the characters which give it individuality. The generally accepted figure of 10 to 15% abnormal of the general population, is evidence that many persons have abnormal E.E.G.s throughout their lives, for which no demonstrable pathological process can be found.

In childhood findings of these kinds are even commoner. Abnormal E.E.G.s have been described by many writers on behaviour problem children. The abnormality is associated with bad temper, irritability and hyperkinesis. Both clinical and electroencephalographic findings are very similar in both the adult and the child. Watterson and I in a previous publication (1942) remarked: "In view of the similarity between the aggressive behaviour of psychopaths and the normal bad temper response to frustration in young children on the one hand, and the similarity between the E.E.G.s of aggressive psychopaths and those of young children on the other, the suggestion that the abnormality in E.E.G.s in these cases is produced by a failure of development in the central nervous system is very tempting." As, however, many behaviour problem children do not become psychopathic adults, one must suppose that a process of maturation does generally occur, but in some cases may be delayed and in some may never be complete.

The process may be disturbed by a pathological lesion. Cerebral trauma and encephalitis in childhood are more likely to result in personality disorder than in the adult. In childhood post-encephalitic behaviour disorder of an aggressive, antisocial character is more frequently seen than Parkinsonism, and behaviour disorder and antisocial conduct are common when the epileptic process appears for the first time in childhood. The general rule that a lesion in a developing organ or system results in greater and more prolonged disturbance of function than with a similar lesion after development is complete, holds good, therefore, when we are considering the development of personality in terms of the central nervous system. It would appear that aggressive behaviour disorder may result from lack of integration in the C.N.S. either from known pathological lesions or from constitutional defect.

COMPARISON WITH EPILEPSY

In idiopathic epilepsy any group or system of neurones can be the site of abnormal discharge. Whether or not the familiar phenomena of major or minor epilepsy appear,

depends on whether the electrical discharge starts in or reaches an area whose function subserves motor or psychic activity. In established epileptics transient motor, sensory or psychic phenomena occur which are the result of epileptic discharge and occasionally organized automatisms are seen which are either the expression of the epileptic discharge itself or follow it as release phenomena from paralysis of neurone function at the highest levels (Penfield, 1941). This distinction is identified by the terms "epileptic automatism" and "post-epileptic automatism". A comparison between dysrhythmics in whom fits occur and those in whom they do not occur may be artificial, particularly if the E.E.G. identification of the epileptic is made on the presence of highly specific wave forms. The absence of spike and wave complexes or fast frequency complexes in the E.E.G.s of psychopaths cannot be accepted as evidence of the non-epileptic nature of the aggressive psychopathic outburst, but only of the reduced probability of *grand mal* or *petit mal* occurring. The comparison of the E.E.G.s of epileptics and D.A.B. patients must be made on other features of the record.

In their original paper on seizure patterns in the E.E.G., Gibbs, Gibbs and Lennox (1938), described, in addition to the two main patterns, a third for psychomotor seizures. In the resting records of such patients, a 6 c/sec. rhythm is frequently seen. This rhythm has the same characters as those we have found in psychopaths. Describing the psychomotor seizures of their epileptics, the Gibbs' (1941) say they may manifest themselves as amnesic states, somnambulism, attacks of abnormal rage, &c. Behaviour is often apparently purposeful, and though usually accompanied by some degree of impairment of consciousness and forgotten after recovery, may be remembered fairly clearly and even justified by the patient. The clinical description might apply equally well to the symptomatology in cases of D.A.B.

We are now in a position to describe the typical E.E.G. pattern in cases of D.A.B. In the present study 80 abnormal E.E.G.s have been analysed for localization of abnormality. 59 (74%) had bilateral post-central 4-6 c/sec. rhythms, and in 49 (61%) this was the only abnormality. It would seem therefore that the bilateral post-central rhythm at 4-6 c/sec. with a voltage approximating to the dominant as a single abnormality correlates very highly with aggressive psychopathic personality disorder (fig. 1).

5-6 c.p.s. Bilateral.
Voltage = D.R.
Poor localization.

4 c.p.s.
Unilateral or bilateral.
Voltage > D.R.
Good localization.
Behaviour disorder severe
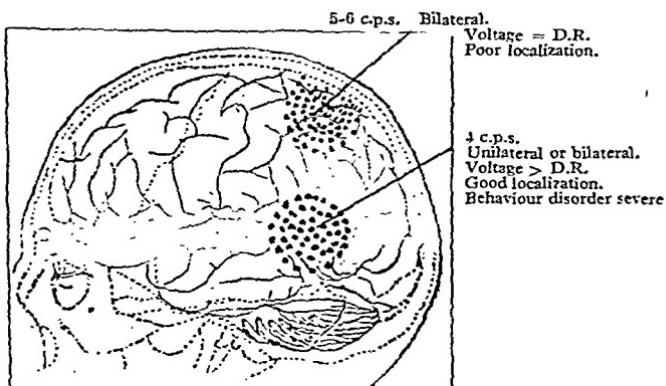
FIG. 1.—Illustrates the difference between the two foci of abnormal potentials described in the text.

By using the transverse electrode placements in a position across the head just behind the ears, the 4-6 c/sec. rhythm can be more easily localized, and two areas for the common appearance of the slow frequencies have been observed (fig. 1). The first is high parietal, and in this area the frequencies are usually faster, nearer 6 c/sec. The other is the posterior temporal regions, and here the frequencies are usually slower, nearer 4 c/sec. and the voltage greater relative to the dominant than in the parietal foci. In the temporal foci there is also a greater tendency for the discharge to be unilateral. The distinction between these two foci of slightly different frequencies is one which has practical significance. While the temporal 4 c/sec. discharge is rarer,

it is also more frequently associated with the more dramatic and severe behaviour disorders (figs. 2 and 3).

Male, aged 18. Irish. Severe head injury, aged 4. Psychopathic family. Brother similar personality. Irresponsible and bad-tempered. Hostile and insubordinate. Has killed three cats by strangulation. Joined Army to find and kill man who "stabbed a brother to death."
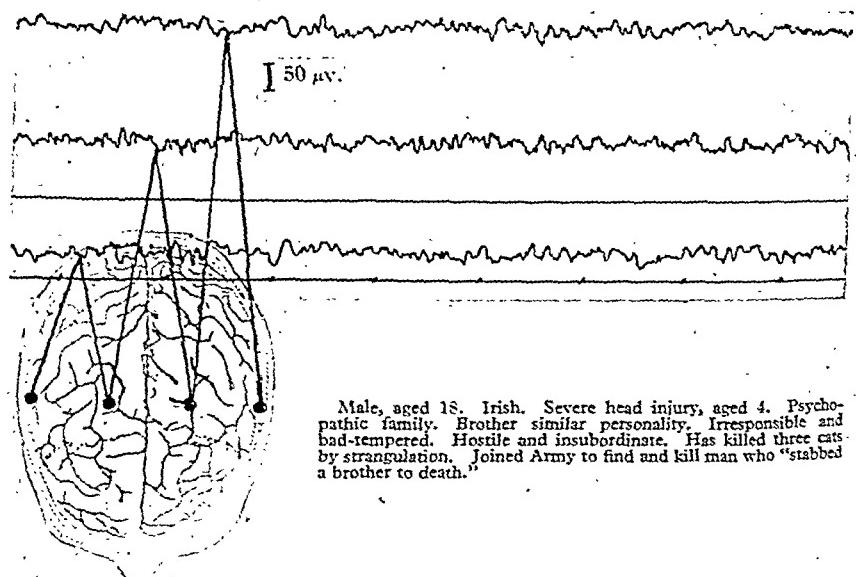
FIG. 2.—Alpha rhythm frequency at 10-11 c/sec. of low voltage; Theta rhythm frequency at 6 c/sec. of medium voltage appearing synchronously and equally on both hemispheres.

Male, aged 21. Examined when on murder charge. Acquitted. Severe behaviour disorder of sadistic, masochistic, and exhibitionist type, with sexual and aggressive features. *No fits.*
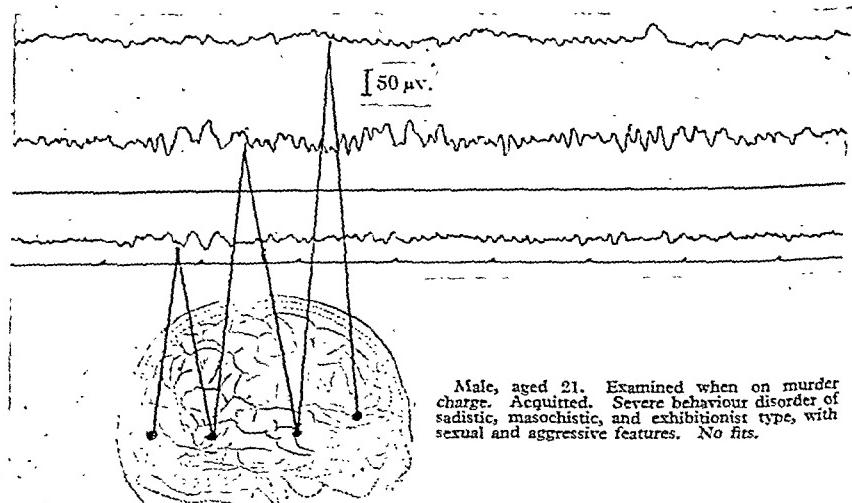
FIG 3.—Alpha rhythm frequency at 9-10 c/sec. of moderate voltage; Theta rhythm at 4 c/sec. of higher voltage focused by phase reversal to the posterior temporal region on the right side.

I have compared the E.E.G.s of 80 cases of D.A.B. with the E.E.G.s of 80 epileptics with major seizures only, 18 epileptics with *petit mal only*, and 8 epileptics with psycho-

motor attacks only. From the table it is seen that epileptics with major fits are, as a

TABLE I.

		Larval	Unilateral 3 c/sec.	Bilateral 3 c/sec.	Bilateral 4 to 6 c/sec.	Fast	△	%
80 D.A.B....	...	2	3	3	65	6	49	(61)
80 major ep.	...	21	13	20	59	16	14	(17·5)
18 minor ep.	...	2	2	2	6	8	3	(16·5)
8 psych. ep.	...	1	1	1	6	3	3	(37·5)

△ = Bilateral 4 to 6 cycle per second post-central rhythm as *only* abnormality.

group, readily distinguished from the D.A.B. cases, by the incidence of "larval" fit patterns, by the frequency of a 3 c/sec. rhythm from one or both hemispheres, and by fast frequencies. The bilateral 4-6 c/sec. rhythm from the post-central regions, which is the commonest feature in the D.A.B. cases (61%), is the sole abnormal finding in' 17·5% of epileptics. So while the typical E.E.G. wave forms of the D.A.B. are to be found almost as frequently in the major epileptics, in the latter they are overshadowed by larval attacks, fast frequencies and 3 c/sec. rhythm. Yet in spite of this, in 17·5% of the major epileptics the E.E.G.s are indistinguishable from those of D.A.B. cases, and in 2 out of 80 D.A.B. patients who had never had convulsive symptoms, larval epileptic electrical phenomena were observed.

The 18 *petit mal* adult epileptics in this series do not differ from the major epileptics in respect of the 4-6 c/sec. rhythm. Little that is definite can be said of the psychomotor epileptics, as there are only 8 of them; but while they have features which associate them with the major and minor epileptics, yet as a group their dysrhythmia is more like that of D.A.B. than of the other two groups. Those with temporal lobe discharges are indeed indistinguishable from D.A.B. cases. A similar difficulty of distinction exists in the clinical field. It all depends on whether the case is regarded as one of "a confusional episode with aggressive behaviour" or "an aggressive outburst with mental confusion". Frequently a diagnosis of epilepsy has been applied to the first but not to the second. The distinction is one of emphasis, and largely subjectively determined.

We may conclude, therefore, that electroencephalographic examination shows strong grounds for thinking that there is a kinship between the D.A.B. patient and the epileptic.

LOCALIZATION OF A RHYTHM WITH BILATERAL SYNCHRONY

Localization of the structural basis for an abnormal discharge may give a clue to function. Recently Silverman (1943) working on criminal psychopaths in America found a similar rhythm to that which we have found in a high percentage of cases. He states that the rhythm is localized to the prefrontal regions. I have certain criticisms of his technique, into which I cannot enter here, but I believe that his results can be reconciled with mine. Where symmetry of a bilateral rhythm is incomplete, Jasper and Kerschman (1941) have shown that the focus of origin may be unilateral, cortical or subcortical and that one hemisphere can drive the other. In most of the cases of the present series a true bilateral synchrony of the 4-6 c/sec. rhythm was present, as was demonstrated by transverse electrodes. It is probable that a subcortical centre is involved in the production of these rhythms, but whether it is itself the site of the abnormal discharge, or whether through its abnormal function it causes the cortex to discharge abnormally is not clear. Dusser de Barenne and McCulloch (1938) state that the normal electrical activity of the sensorimotor cortex depends upon the influx of thalamocortical impulses and numerous workers have shown that lesions of the thalamus and thalamocortical radiations will abolish all rhythmical cortical frequencies, yet if 1 sq. cm. of cortex is left in functional connexion with the thalamus, spontaneous rhythmic activity can be obtained from it (Dempsey and Morrison; 1942). Obrador (1943) produced acute lesions in the hypothalamus and base of the brain in anæsthetized cats and found that this abolished the rhythmical cortical frequencies. He also confirmed that lesions of the thalamus and thalamocortical pathways had a similar effect, but that section through the mid-brain had not. He suggested from these experiments that the hypothalamus may influence cortical activity through its thalamic connexions.

HYPOTHALAMIC STIMULATION

A few workers have recorded the E.E.G. from a basal lead, either resting against the roof of the nasopharynx or by means of a needle electrode passed through the nose and embedded in the basal portion of the sphenoid bone. Using this method on cats and

human subjects Grinker and Serota (1938) recorded potentials which were undoubtedly the result of activity in the hypothalamic nuclei. This can be claimed from the results of electrical stimulation through the embedded electrode. These workers observed that the most characteristic rhythm of the hypothalamus in cats and man is a 4·5 c/sec. rhythm. Comparison of cortical and basal potentials was made under varying conditions. Ordinary electrical stimulation increased the voltage of hypothalamic potentials immediately and the increased potentials recurred in bursts for long periods afterwards. The similar effect, observed in the cortical E.E.G., was thought to be secondary to the discharge in the hypothalamus. Very strong electrical stimulation to the hypothalamus produced massive discharge which appeared synchronously in both hypothalamus and cortex. These workers also made an interesting experiment; they found that a severe emotional stimulus—they told their subjects that masturbation had irreparably damaged them—produced discharge in cortex and hypothalamus similar to that produced by electrical stimuli. In considering their results, Grinker and Serota make the following observations: "Stimulation of the hypothalamus evokes a massive discharge which persists or reappears for minutes after stimulation is over. This suggests that this structure serves as a reservoir for prolonged excitation and has a chronic influence on brain and periphery. Affect-laden ideational stimuli similarly cause hypothalamic excitation which precedes and outlasts the cortical ones. The results indicate a 'driving' of the cortex by hypothalamus parallel to the well-recognized overwhelming of intellectual processes by emotional activity."

The best-known pathological rhythm with bilateral synchrony is the 3 per second wave and spike complex of *petit mal*. There can be no doubt that in many cases this rhythm is controlled by a deep pacemaker. Jasper and Penfield (1941) by placing electrodes along the base of the brain at an operation on a child were able in the following twenty-four hours to demonstrate a point on the mid-hypothalamus between the infundibulum and the mammillary bodies from which they could obtain phase reversal for the spike and wave complex and electrical stimulation of which resulted in many of the vegetative phenomena of the fit. This area, therefore, behaved like an area of epileptogenic cortex, and was responsible for the initiation and control of the bilaterally synchronous discharge. Jasper also considers that the bilaterally synchronous 6 cycle rhythms "arise in some deep-lying or mid-line structures". He states that patients with prominent 6 cycle rhythms have behaviour automatisms, and with Solomon and Bradley (1938), he considered that the behaviour problem children who showed this rhythm were "epileptoid". It appears, therefore, on electroencephalographic evidence alone that bilaterally synchronous 6 cycle rhythms have a deep origin, and Jasper considers that the amount of bilateral synchrony in an abnormal frequency is a measure of the depth of the lesion in the brain.

In four cases of suprasellar tumours, on which Dr. W. Cobb had performed E.E.G.s bilaterally synchronous 4-6 c/sec. rhythms appeared in the E.E.G., but the symmetry was particularly well shown in two cases—one man and one woman in whom hypothalamic vegetative symptoms were marked. It is probable that in these cases numerous areas of grey matter in the floor and walls of the 3rd ventricle were pressed upon by the growing tumour, and it would be unwise to postulate any particular nucleus or nuclei as the site of disturbance for the slow electrical discharge seen in the cortex. It seems more probable that this frequency band, the 4-6 c/sec. band, or "Theta" band as Grey Walter has named it, is intimately concerned with the functions of the basal grey matter and is to be observed from cortical electrodes wherever the functions of this grey matter are disturbed.

Cairns *et al.* (1941) reported a case of epidermoid cyst of the 3rd ventricle which when tapped on three occasions always resulted in rapid return of normal consciousness and responsiveness. The patient, a girl of 14, showed a condition of "akinetic mutism". She was devoid of all emotional expression, even to a strong painful stimulus. She would follow people with her eyes, but was mute. Within a few minutes of the cyst being tapped, she sat up and said "Where am I?" Whitteridge recorded the E.E.G.s of this case on two occasions before and after the cyst was tapped. He found irregular slow discharges of high voltage from both hemispheres at a rate of 1-3 c/sec. and interspersed by periods of nearly sinusoidal discharge at 2-5 c/sec. These appeared to be symmetrical and synchronous on the two hemispheres. The authors showed that these abnormal waves were not the result of raised intracranial pressure but of hypothalamic dysfunction, and postulated an interference with the periventricular system of fibres. They remarked that the evidence in the case showed clearly "that the cortex was largely put out of action by local pressure at the diencephalic level" which suggests "normal cortical

activity depends not only on afferent impulses from the outside world, . . . but also on some other impulses mediated by the diencephalon".

It can be said, therefore, that there is strong presumptive evidence that the bilateral rhythmic disturbance in the E.E.G.s of D.A.B. cases is associated with dysfunction of basal grey matter, probably thalamus or hypothalamus or in circuits of neuronal chains which connect the two.

At this point, it is pertinent to the problem to review briefly the associations between hypothalamic functions and aggressive behaviour. In the experimental field much work has been done since Goltz in 1892 demonstrated that the decorticate dog showed irritability and anger after slight and innocuous stimuli.

Investigations have been directed towards finding which parts of the fore-brain must be ablated to induce the rage response. Bard (1928) has demonstrated the response in cats in which the cerebral hemispheres, corpora striata, and cranial half of the hypothalamus have been removed. Fulton and Ingraham (1929) evoked the same response by an incision in front of the supra-optic hypothalamic nuclei. The lesion must be bilateral. It is suggested that the vegetative component of the rage reaction is a release of the posterior hypothalamus; and the somatic component a release of the tegmental grey matter of the mid-brain. Spiegel, Miller and Oppenheimer (1940) could not elicit rage responses from ablations of the neopallium, but if frontal pole extirpations encroached upon the olfactory tubercles, or if these areas were the site of isolated lesions, then "sham rage" followed.

Perhaps the hypothalamus and related nuclei are the structural foundation for emotional experience as well as for emotional expression, but of the latter there can be little doubt. It is to be observed that apathy, listlessness, absence of emotional responsiveness and initiative—the opposite to aggressiveness—are as readily induced as aggressiveness by basal lesions.

It has been suggested that the stab lesions of Fulton and Ingraham anterior to the supra-optic nuclei possibly divided cortical inhibitory paths, since it is known that the frontal cortex sends fibres having inhibitory influence to the septal nuclei, to the dorsomedial thalamic nucleus, and to the zona incerta, where they are relayed to the posterior hypothalamus (Clark, and Boggon, 1933). While exercising due caution when making comparisons from the results of animal experiments with human behaviour, it would seem that in man, the influence of the olfactory apparatus is less and that the inhibitory effects of discharge from the area granularis of the prefrontal cortex on the hypothalamic-thalamic function is more important. Reasons for this are to be found from the second source of data, namely, from recorded clinical observations.

THE HYPOTHALAMUS AND BEHAVIOUR

Riddoch (1938) in discussing the clinical aspects of hypothalamic function remarks upon the rarity of states of excitement in the course of chronic diseases and slowly developing lesions of the hypothalamus and considers that such states "are a response to acute disturbance of function, to sudden release from cortical control". He also remarks that "it is possible that the thymic make-up of the individual" determines whether or not emotional reactions will readily follow diencephalic lesions. However this may be, it is the acute conditions which tend to result in the excited or positive reaction, though the unstable affectivity of disseminated sclerosis and pseudobulbar palsy is, in Riddoch's opinion, due to release of the hypothalamus from cortical control. As already mentioned, the disease which can most nearly parallel the symptomatology of D.A.B. is encephalitis lethargica occurring in childhood, in which the pathological process is largely confined to the peri-aqueductal grey matter, substantia nigra, and to a certain extent in the walls of the 3rd ventricle. I would emphasize again the effect of this infective condition on the developing brain and contrast it with the effect in the adult brain: while the lesions are the same, the effect is different. In the child the process of maturation, reflected in the changing frequencies of the E.E.G., or in Hughlings Jackson's terminology, "integration", is still in progress. Foster Kennedy (1940) remarks on the incidence of temper tantrums, lying, stealing, arson, among young people with functional hypothalamus signs as being more frequent than in physically normal persons.

Cushing (1929), who first remarked on the indifference and apathy in cases of craniopharyngioma, contrasted this picture with the violent and aggressive behaviour in a girl of 13 following operation for glioma of the optic chiasma. Alpers (1937) described a personality change in a man of 39 with teratoma of the 3rd ventricle destroying the hypothalamus.

"A year before signs of tumour developed he became irritable, hypersensitive, aggressive, argumentative, curt, stubborn and unreasonable. He frequently flew into a rage over trivial matters."

Post-mortem revealed extensive destruction of the hypothalamus except some of the posterior nuclei.

In connexion with the influence of frontal lobe control, the following case of Dott's is important. He wrote:

"In lesions involving the frontal lobe, especially on the left side close to the hypothalamus, where the fronto-hypothalamic bundle converges, the mood and emotional make-up may resemble those of a wild and ferocious animal. We saw a boy of 4 years who sustained a laceration with an abscess extending deeply into the posterior part of the orbital surface of the left frontal lobe. Formerly a cheerful friendly child, he settled into a state of dull morose anger. Alert and fully conscious, he would not speak nor co-operate in any way. Given a formerly beloved teddy bear, he slowly tore it limb from limb with deliberate and ferocious savagery. He was actively aggressive if approached. When his abscess was cured, he became his former pleasant and well-behaved self."

These two cases demonstrated sudden attacks of rage and aggressiveness. There was no question of an epileptic process, but in another two, described by Vonderahe (1940) and Sjöqvist (1941), an epileptic process was undoubted, in the one stimulated by new growth and in the other by a traumatic lesion.

The following two cases illustrate the difficulty of making on clinical grounds or any other, a distinction between the outbursts of epilepsy and D.A.B. Both these men are criminal psychopaths and at the time of examination were serving sentences in prison.

CASE I.—A young man of 20 was seen at the request of Dr. Young, Senior Medical Officer of Wormwood Scrubs. He was serving a sentence of three years for arson, which he had committed, in his own words, "to draw attention to himself". He was the eldest boy of four siblings, one of whom had infantile convulsions. He had always had a vile temper, was egocentric, and had shown depressive mood swings. His mental age was 11. At the age of 12 he had suffered head trauma of moderate severity. His attacks of violence had, however, dated since childhood and at school he was regarded as a "border-line mental case" because of them. The attacks of violence were very severe, almost homicidal in character, but were not associated, as far as could be ascertained, with loss of consciousness. The attacks were precipitated by minor frustrations and at the onset he would experience paræsthesia and tremor of the left leg. Having made his assault, he would feel relieved. On one occasion he had attacked an officer of the prison and on another he had been found in his cell in a "collapsed condition". No details of this are available. No abnormal physical signs were detected, but the E.E.G. was abnormal, particularly on the right cortex, which showed irregular slow frequencies, the most obvious of which was at 4 per second. The E.E.G. was unstable to hyperventilation. There seemed little doubt that a traumatic factor was present here, though the temper and attacks antedated the trauma. Here we had evidence then of aggressive personality disorder and homicidal assaults, but there were symptoms suggesting post-traumatic epilepsy.

CASE II.—Another young man of 21, ex-Borstal boy with previous prison sentences for larceny and for insulting behaviour, was seen at the request of Dr. Norris, of Feltham Prison. The patient was serving a sentence for breaking and entering. His mental age also was 11 years. He was a tall powerful man with acromegaloid features, but no definite evidence of a pituitary lesion. His family history was clear. He also had suffered a head injury of moderate severity. In prison he was well liked, and was amiable and quite affectionate towards the staff. He was sent for an E.E.G. because for some years, since his head trauma, he had exhibited attacks of violent behaviour in which he carried out apparently volitional acts such as throwing about movable articles and was aggressive if approached. He professed complete amnesia for these attacks, which were preceded and followed by intense frontal headaches. Mixing with others appeared to increase the attack frequency, while phenobarbitone reduced it and also the intensity of the episodes, the duration of which varied from two to ten minutes. It was thought that to some extent the development of the attack was within the patient's control. Prior to confinement in prison he had made a half-hearted attempt at hanging himself, but whether associated with an attack or not was unknown. No abnormal physical signs were elicited; his E.E.G. was abnormal. The alpha frequency showed great variability and there was a 6 c/sec. discharge from both parieto-occipital regions. While the E.E.G. was being taken the patient had a partial convulsion. This consisted of apparent sudden loss of consciousness, with flushing of the face. There was tonic spasm of the arms, and the head and eyes turned to the right. The E.E.G. was being observed from the post-central regions at the time, but no new rhythmical frequencies appeared, such as are usually associated with an epileptic process, though not necessarily with one primarily involving the vegetative and postural centres. All further physical investigations proved negative, and the psychotherapeutic study in prison suggested that the attacks were hysterical. After this he remained free from attacks for a month and was then released from prison.

The diagnosis made was "hysterical manifestations in a subnormal aggressive psychopath".

IMPAIRMENT OF CONSCIOUSNESS

There is little doubt that dangerous assaults are committed in full consciousness and with malice aforethought by cases of D.A.B. as well as by epileptics. Indeed it is probable

that psychopathic persons purposely transgress in this manner more frequently than non-psychopathic persons. But in many unpremeditated impulsive assaults, the history indicates a partial or complete amnesia or some curious features of the accused's account of the crime or the manner in which he committed it. It is generally believed that amnesia for a series of events is invariable where epilepsy is present and that absence of amnesia— the capacity to give a more or less factual account of events—is strong evidence against epileptic discharge having occurred. This belief is probably true in the severe para- lytic phase following a *grand mal* convulsion; it is very far from the rule in psychomotor epilepsy in which the behaviour disorder occurs concurrently with or follows the elec- trical discharge. In such cases there is frequently a very good memory for objective events as well as the bizarre subjective experiences which usually occur. In these cases the presence of subjective experiences—unreality feelings, uncinate phenomena, and hallucinations—are more diagnostic of epilepsy than any impairment of consciousness which may be associated. Since, as our results seem to indicate, the focus for abnormal function in D.A.B. is usually in basal or deep temporal grey matter, if epileptic discharge accounts for some of the assaults in these cases, then severe impairment of consciousness is not to be anticipated. The following case illustrates the concurrence of epileptic behaviour disorder with no amnesia.

CASE III.—A young soldier, aged 22, was admitted to Sutton under Dr. William Sargant, on 18.1.42: on that day had been observed at his unit in two generalized epileptic seizures. He had only been in the Army a week and his history revealed that he had suffered from major and minor fits since childhood. No epilepsy or psychopathy had occurred in his family. On admission he said he felt dazed and tired, but the next day he improved and remained co-operative and friendly, without objective symptoms until January 22, that is four days later. On this day he began to behave in a strange manner. He appeared bright and inconsequent, but was normally oriented in time and place. He said he felt strange and unreal, had a roaring noise in his ears, and saw coloured lights. He mistook the fire bell for a sign for him to come out of his "coma" as he called it and he held his thumb in a certain position to allow the electricity to run up his arm. He also heard God speaking to him. His mental state led a competent psychiatrist to consider him schizophrenic. The next day he became restless and had to be removed to Banstead Mental Hospital, where he had to be placed in the "pads" for twelve hours. He then began to improve, but in his own statement it "was two or three days before I was com- pletely round". Thus it would appear that this psychotic episode lasted at least four days. He was later readmitted to Sutton, where routine E.E.G. tests for establishing control of his dysrhythmia by anticonvulsants were made and he finally left hospital much improved. When last heard of he had been free from fits for eighteen months. The patient who had a mildly aggressive personality and easily flared up, wrote out for us an account of his experiences during this psychotic episode which reveals that he had complete memory for all the events leading up to, and throughout the attack. He details time, individuals, and the manner of his admission to Banstead, and his recovery.

This man's E.E.G. was grossly abnormal. A high voltage 4 c/sec. rhythm was found in both temporal lobes, and the hyperventilation elicited the spike and wave complexes of *petit mal* which occasionally could be observed clinically. It must be emphasized that this psychotic episode could not be regarded as secondary to the two fits which he had had five days previously. He had recovered from these and had performed an I.Q. test which gave him an average intelligence, which was not significantly lower than another test three months later when he was fully stabilized. A study of his state and his story suggests, in my opinion, that the first part of the episode was associated with epileptic discharge, probably in a temporal lobe. He had unreality feelings, heard deafening bangs and a roaring noise, saw flashes of light and felt electricity moving up his right arm. He was also aurally and visually hallucinated. This state, which suggests a slow- moving discharge, suddenly ceased with an acute ecstatic experience. Thereafter no further sensory or uncinate phenomena occurred, but the state changed to one of rest- lessness with paranoid delusions and mistaken interpretation of environmental experiences, in which he felt he had a duty to kill Hitler. It suggests that this latter part was a release phenomenon after the epileptic discharge was over, the general integration of cerebral function being still abolished through the paralysis of those neurones which had been the channels of the discharge. We have in this episode an undoubted epileptic or post-epileptic automatism for which complete memory is retained.

There is little doubt, in my opinion, that however complete memory for a D.A.B. outburst may or may not be, some evidence of impairment of consciousness is frequently found. In thinking of degrees of consciousness we must consider a scale which has coma at one end, with responsiveness to severe painful stimuli next, then stupor in which responsiveness is more readily though briefly available, through types of unconsciousness in which complex motor behaviour of a quasipurposive kind can occur, to dazing with patchy amnesia, and finally to the finest grades of impairment of consciousness, in which judgment and the capacity for complicated reasoning are alone impaired. Paterson (1942) has shown in his studies of recovering head injuries

that the many functions upon which consciousness depends can be knocked out selectively. When any single function is so paralysed, there is a restriction of the background of mental activity specific to that function. Thus after head injuries he found that "a restriction of conscious activity to a few aspects only of a situation and to isolated emotional attitudes" was common. The case of a recent murderer, who was seen through the kindness of Dr. Grierson, illustrates this.

The young man, who had always had a vile and dangerous temper, was ill-adjusted socially and sexually. He killed a young woman and her 2-year-old child suddenly by repeated blows on their heads with a coal hammer. He did this in the presence of his own wife. No serious quarrel had occurred and there was negligible motive. Though he had drunk a good deal of beer previously, there was no evidence that he was grossly intoxicated. Asked why he did it, he said: "I thought what an evil woman she was", and regarding the infant he said: "I heard the baby crying in the other room and thought the child won't be any good without the mother." He denied other feelings than these. An E.E.G. showed the usual abnormalities, and undoubtedly he was a case of D.A.B., but there were no features to lessen his responsibility in law, and he was condemned and executed.

To account for this sudden blunting of sensitiveness, this restriction of the conscious field, we must look at that quality which cases of D.A.B. share with dysrhythmic epileptics, namely, their cortical electrical instability to chemical stresses. My colleague, Dr. Heppenstall, working on a hyperventilation sensitivity test, has shown that while the hyperventilation response of neurotics and traumatic cases invariably becomes normal when the blood sugar is artificially raised above 150 mg.%, this is not the case with epileptics and some cases of D.A.B. This is then another sign of the biological affinity of these two groups.

Hypoglycæmia as a cause of increased cortical sensitivity to hyperventilation has been reported by Davis and Wallace (1942); with Dr. Sargant and Dr. Heppenstall (1943) I
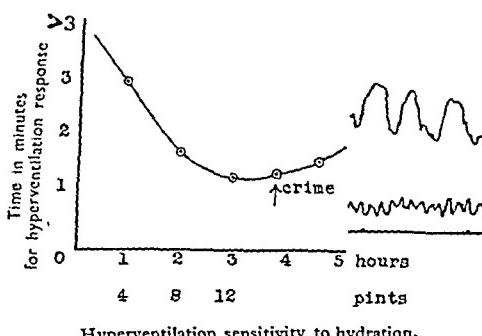
Hyperventilation sensitivity to hydration.

CHART.—This curve illustrates the increasing sensitivity to hyperventilation induced by hydration. This was the case of a man executed for murder, which he committed 40 minutes after drinking 12 pints of beer. The short tracings on the right illustrate the difference between his resting E.E.G. and after hyperventilation (*above*).

reported a case some months ago. The alkalosis of hyperventilation in the presence of hydration is probably much commoner in D.A.B. assaults.

Hydration which precipitates epileptic fits, also increases the brain's sensitivity to hyperventilation. Indeed, the greater the degree of hydration, the more readily does the E.E.G. become unstable to hyperventilation (Chart). This was also shown to occur with hypoglycæmia in the case of matricide already referred to. Rapid raising of the blood sugar after considerable hydration had occurred, abolished the cerebral instability and we were of the opinion that in that particular case hypoglycæmia rather than hydration was the significant factor. No doubt the two factors can coexist, either supplementing or cancelling the effect of each other. Thus, a high blood sugar will protect the brain from the effects of hydration. In criminal assaults it is probable that hydration is a commoner factor than hypoglycæmia. This, as a result of alcoholic excess, is supplemented by the influence of alcohol itself—another factor which depresses the highest cortical function yet increases dysrhythmia.

It is apparent then that the physiological stresses so frequently observed preceding aggressive outbursts in cases of D.A.B. are in fact just those factors which are likely either to induce cortical discharge or to increase the sensitivity of the brain to hyperventilation.

The instability of the E.E.G. to hyperventilation alkalosis is a non-specific reaction and appears as a bilaterally synchronous slow discharge, in which a very high voltage 3 c/sec. rhythm is the most prominent, seen first in the most anterior part of the frontal lobes, spreading back to all cortical areas as the condition progresses. It would be generally agreed that nerve elements which are suddenly involved in such an oscillating system must inevitably have their function impaired. Davis and Davis (1939) reported partial clouding of consciousness with the appearance of these large slow potentials, and Davis and Wallace (1942) more recently, found amnesia, confusion and vagueness for stimuli given to their subjects during such periods. The hyperventilation of intense excitement or a struggle in which the hyperventilation is not chiefly the result of muscular exertion, will, therefore, if sufficiently prolonged, induce cortical instability affecting the prefrontal areas first. Our testing suggests that amnesia is only evident when the discharge has involved the whole cortex. The inference can, I think, be drawn that the first appearance of hyperventilation instability would involve the function of those cortico-hypothalamic fibres whose inhibitory influence has been traced, as Le Gros Clark (1938) points out, to the posterior hypothalamus. Removal of this chief source of cortical control might, under suitable conditions of emotional stimulation, result in discharge of the posterior hypothalamus which Bard (1928) considered the vegetative component of the rage response. Such an explanation gains support from the evidence which suggests an overactivity and degree of autonomy in this area.

RECAPITULATION

Some recapitulation is perhaps desirable at this point. In emphasizing the physico-chemical abnormalities of constitution which form the background of cerebral function in cases of D.A.B., I have made no mention of psychological factors either in reference to the developing personality or when considering the aggressive outbursts. This paper has been solely concerned with these physical factors, but I should be doing both my subject and myself an injustice if I suggested that with these matters alone a formulation of ætiology could be made. This is obviously not so. Each individual personality with its particular drives, aversions, emotional preoccupations and fears, and its capacity for adaptations in the various fields of human affairs is inevitably the result of particular interaction of the developing organism with the environment. No doubt the effects of such interaction are built into the personality and become an influence on future behaviour—a process which in physiological terms is best called "conditioning". No doubt the broken home, the violent-tempered parent, the early psychic trauma play their part in this conditioning, but at the same time the question should be asked: "Why does the parent have a violent temper and break up his home: is his behaviour also the result of early stresses or are father and son both 'tarred with the same genetic brush'?" As Maudsley said: "Can a man escape from his ancestors?"

The problem of whether the cerebral dysrhythmia in these cases is of the same hereditary type as Lennox, Gibbs and Gibbs (1940) have found in the convulsive epilepsies is important. It forms the subject of other investigations which are incomplete, yet the evidence both clinical and electroencephalographic suggests that it may be so.

I will return now to those two considerations with which I commenced, namely, the development of the personality and the nature of the attack. In respect of the first, there is good reason to believe that from the earliest years an abnormal state of electrical pattern exists in the brain and that when adult life is reached, the functional abnormality is probably in those basal areas of grey matter that are particularly concerned with the reception of crude sensation and with emotional expression. It suggests a degree of autonomy of function in thalamic-hypothalamic circuits. At this point it is tempting to speculate on a failure of development in central nervous function, using the Jacksonian concept of "integration" as the essential process, and postulating a failure of cortical inhibitory control of that hypothalamic activity which is concerned with the vegetative responses to emotional stimulation. At the present time such a theory is however only speculative when it is applied to personality structure: but these investigations suggest that the aggressive outburst, when it is not the expression of epileptic discharge itself, may be frequently a release phenomenon from an acute failure of cortical inhibition. Here Hughlings Jackson's concept of "dissolution at the highest level" seems applicable. The readiness with which this dissolution occurs can be measured in terms of E.E.G. sensitivity to hyperventilation; such sensitivity being increased by physicochemical factors. Hydration and hypoglycæmia are at present known, but undoubtedly there are others. Further, this hyperventilation sensitivity of the E.E.G. and the abnormal characters in the spontaneous record are of the same order of cerebral dysfunctions as the dysrhythmia which is indicative of the convulsive tendency.

The differences between the cerebral events in motor seizures and the cerebral events in aggressive outbursts are perhaps best sought in the site of discharge, its time relations, and the degree of spread to other areas.

The biochemical investigations forming the basis for part of this paper were carried out in collaboration with Dr. Mollie Heppenstall and Dr. William Sargant, to whom I am much indebted. It is also a pleasure to express my indebtedness to many colleagues at Sutton who have allowed me to examine their patients, and also to Dr. Hugh Grierson, Dr. H. T. P. Young, and Dr. J. C. M. Matheson of H.M. Prison Service, to Colonel A. A. W. Petrie and the medical officers of Banstead Military Hospital, and to Dr. W. Cobb for permission to refer to his cases. I have received invaluable criticism and advice from Dr. Eliot Slater, Dr. George Dawson, and Dr. Alfred Meyer. Mr. J. Theobald, electroencephalographic technical assistant, has taken many of the records. Lastly, I am indebted to Dr. Louis Minski and the Research Committee of the L.C.C. Mental Hospitals for the facilities to carry out this work, as well as to the Rockefeller Foundation for apparatus and support.

REFERENCES

ALPERS, B. J. (1937) *Arch. Neurol. Psychiat.*, Chicago, 38, 291.
BARD, P. (1928) *Amer. J. Physiol.*, 84, 490.
BLEULER, E. (1934) Textbook of Psychiatry. New York.
CAIRNS, H., OLDFIELD, R. C., PENNYBACKER, J. B., and WHITTERIDGE, D. (1941) *Brain*, 64, 273.
CLARK, W. E. LE GROS, BEATTIE, J., RIDDOCH, G., and DOTT, N. M. (1938) The Hypothalamus. Edinburgh.
———, and BOGGON, R. H. (1933) *Brain*, 56, 83.
CUSHING, H. (1929) The Pituitary Body and Hypothalamus. Springfield.
DAVIS, H., and DAVIS, P. A. (1939) *Ass. Res. nerv. ment. Dis.*, Proc. (1938), 19, 50.
———, and WALLACE, W. McL. (1942) *Arch. Neurol. Psychiat.*, Chicago, 47, 606.
DEMPSEY, E. W., and MORRISON, R. S. (1942) *Amer. J. Physiol.*, 135, 293.
DUSSER DE BARENNE, J. G., and McCULLOCH, W. S. (1938) *J. Neurophysiol.*, 1, 364.
FULTON, J. F., and INGRAHAM, F. D. (1929) *Amer. J. Physiol.*, 90, 353.
GIBBS, F. A., and GIBBS, E. L. (1941) Atlas of Electroencephalography. Boston.
———, ———, and LENNOX, W. G. (1938) *Arch. Neurol. Psychiat.*, Chicago, 39, 298.
GOLTZ, F. (1892) *Pflüg. Arch. ges. Physiol.*, 51, 570.
GRINKER, R. R., and SEROTA, H. (1938) *J. Neurophysiol.*, 1, 573.
HENDERSON, D. K. (1939) Psychopathic States. London.
HILL, D., SARGANT, W., and HEPPENSTALL, M. (1943) *Lancet* (i), 526.
———, and WATTERSON, D. (1942) *J. Neurol. Psychiat.*, 5, 47.
JASPER, H. H., and KERSCHMAN, J. (1941) *Arch. Neurol.*, Paris, 45, 903.
———, and PENFIELD, W. (1941) *See* Penfield and Erickson.
———, SOLOMON, P., and BRADLEY, C. (1938) *Amer. J. Psychiat.*, 95, 641.
KENNEDY, F. (1940) *Res. Publ. Ass. nerv. ment. Dis.*, 20, 864.
LENNOX, W. G., GIBBS, E. L., and GIBBS, F. A. (1940) *Arch. Neurol. Psychiat.*, Chicago, 44, 1155.
MAUDSLEY, H. (1873) Body and Mind. London.
OBRADOR, S. (1943) *J. Neurophysiol.*, 2, 81.
PATERSON, A. (1942) *Lancet* (ii), 717.
PENFIELD, W., and ERICKSON, T. C. (1941) Epilepsy and Cerebral Localisation. London.
SILVERMAN, D. (1943) *Arch. Neurol. Psychiat.*, Chicago, 50, 18.
SJÖQVIST, O. (1941) *Acta chir. scand.*, 85, 235.
SPIEGEL, E. A., MILLER, H. R., and OPPENHEIMER, M. J. (1940) *Trans. Amer. neurol. Ass.*, 66, 127.
VONDERAHE, A. H. (1940) *Trans. Amer. neurol. Ass.*, 66, 129.
WALKER, A. E. (1936) *J. comp. Neurol.*, 64, 1.
WALLENBERG, A. (1934) *Jb. Psychiat. Neurol.*, 51, 295.

Dr. A. A. W. Petrie said he had followed these investigations with great interest. This section of the work had been mainly done on criminals and avowed psychopaths. Many of even the aggressive psychopaths also showed inadequacy and quite a number showed actual mental deficiency. He thought that a series of electroencephalograms on the higher-grade mental defectives especially of the unstable type would be of great interest and might show a correlation with the results obtained among the criminals and psychopaths and even indicate that all these persons were virtually members of the same group.

Wing-Commander Denis Williams: The results of work, notably in America, upon psychopathic and psychotic individuals, and upon children who present behaviour problems, have suggested that a cerebral dysrhythmia is the expression of a basic constitutional instability in them. Figures published three years ago (Williams, 1941) related to these earlier results seemed to indicate that even in normal subjects, a cerebral dysrhythmia had the same significance. I wrote that: "An abnormal E.E.G. indicates an inborn constitutional defect which may find expression as epilepsy or a behaviour disorder such as a constitutionally determined psychoneurosis, psychopathy, or psychosis, in the subject himself or his children." Although this statement was criticized at the time, subsequent observations have lent increasing support to it. It is, however, simply concerned with abnormal E.E.G.s in general, and not with any specific kind of abnormality.

More recently (Williams, 1944) evidence has been accumulated which seems to show that intermittent, paroxysmal changes in the E.E.G. of the sort characteristically seen in association with epileptic attacks have a similar, though specific relationship to an epileptic tendency. Experimental work, accumulated data, and clinical observation all indicate that in subjects whose behaviour is otherwise normal, these episodic disturbances in the E.E.G. indicate either an inborn or an acquired tendency to epilepsy (Williams, 1944). This being so it is interesting to find that some subjects who show periods of impulsive aggressive behaviour without amnesia, and in the absence of convulsions may have similar changes in the E.E.G. It is not suggested that the presence of amnesia is necessary for the diagnosis of epilepsy, or that purpose may not be evident in the destructive outburst of the epileptic. The individuals whom Dr. Denis Hill has described could not, however, by any stretch of the imagination be called "epileptic" if this term is to have

any reasonable meaning in clinical medicine. The cases, on the contrary, fall quite clearly into the group of aggressive psychopaths, which has been described at length by him and Watterson. The evidence to which I have referred suggests, nevertheless, that there is very little difference between the basic disorder—whether it is biochemical or physical—which is responsible for the abnormal behaviour of an aggressive psychopath and of an aggressive epileptic, and it is very suggestive that Dr. Hill has arrived at this conclusion from the study of a large number of psychopaths while I have done so from a study of epileptics. The following case illustrates how closely the E.E.G. of subjects with episodes of purposive aggressive behaviour which they are able to recall may simulate that of an epileptic.

A lance corporal, aged 29, had had a severe closed head injury, with an amnesia of two and a half hours, five months before admission to a hospital for head injuries. He came in because of a mild post-traumatic state, with headaches, lack of concentration and depression, as well as irritability and violent fits of temper. He had always been quick tempered and aggressive, but had avoided serious social consequences and had been a reliable workman and a satisfactory family man before the accident. In hospital he would show uncontrollable rage at very slight provocation. For instance, he nearly struck the medical officer in his exasperation at being unable to perform an intelligence test, he threw a mug of water into the face of a patient who had taunted him, screamed at the nurse and later the sister who came to pacify him, and had to be restrained. Similar episodes were frequent. His family history showed that his father and paternal uncle had similar outbursts. His father had thrown him into a canal in fury when he was a young child, was a chronic alcoholic, and used to beat his children uncontrollably. His uncle had attacked his wife with a knife on several occasions.

There were no physical sequelæ of the head injury and it was thought that the outbursts of rage were at most accentuated by it. The man was a mild psychopath of the aggressive type, with a strong family history of this nature. He had never had any attacks of unconsciousness, and he and his relatives always had memory and remorse for their explosive aberrations of behaviour. The patient's resting E.E.G. shows episodes of high voltage 3 and 4 a second waves which are indistinguishable from those seen in epileptics.

Although it may prove necessary, as Dr. Hill has shown, to consider psychopathic behaviour as closely related to epileptic behaviour, it would be unwise to extend the use of the term epilepsy. It means a seizure and it has very real social and economic implications which cannot be disregarded. Lennox has suggested the expression "cerebral dysrhythmia", but this implies that the cerebral electrical disturbances are the cause of the behaviour disorder, and not its accompaniments. In relation to the relatives of epileptics and the patients with a cerebral lesion and who show an episodic dysrhythmia of an epileptic kind, I have suggested the term "latent epilepsy", as opposed to "active epilepsy". It is imperative to avoid the use of clinical terms to describe E.E.G. phenomena but in this borderland between psychopathy and epilepsy which Dr. Hill has demonstrated to us, the present terminology is quite inadequate.

Reference.—WILLIAMS, D. (1941) *J. Neurol psychiat.*, 4, 257 ; (1944) *Brain* (in press).

Dr. William Sargant said he had been able to take part in the investigation of biochemical problems relating to the E.E.G. in America before the war and also at Sutton with Dr. Hill. He was sure that Dr. Hill's work and other work going on now in America would revolutionize many of our conceptions and treatment of certain forms of aggressive violence. He (Dr. Sargant) had sometimes seen the release of uncontrolled aggressive behaviour in such patients, when they happened to get placed on insulin treatment and the blood sugar became lowered prior to the onset of coma. In one patient, with the E.E.G. findings described by Dr. Hill, violent behaviour had been accompanied by a state of consciousness in which the patient still knew what he was doing and that it was wrong and even apologized for being unable to control himself while he was doing it. Raising the blood sugar rapidly abolished the abnormal behaviour and restored the power of self-control.

He believed that Dr. Hill's paper carried with it some important general implications Many apparently normal members of the population had abnormalities of E.E.G. function as part of their inherited make-up. They only needed certain biochemical and environmental stresses to turn them into criminals and impulsive murderers. Such stresses were more frequently met with in wartime with the prevalence of concussional and blast effects on the brain, the tendency to excessive hydration of the cerebral cortex due to the increased consumption of weaker beer, the relaxation of cerebral inhibition due to other forms of alcohol, and the physical deterioration and loss of weight which occurred with prolonged fighting and other unavoidable war stresses. Disaster was going to occur to previously respectable citizens subjected to such stresses through no fault of their own. They would eventually "fire-off" into an aggressive impulsive act with an environmental stimulus that in normal times would leave them unmoved. An increase in crimes of violence among ordinary citizens could be confidently predicted as the war progressed and for some time afterwards on the basis of these findings.

The question of treatment was most important. A hundred years ago we believed that flogging, strait-jackets and handcuffs were the treatment of lunacy. They were thought to be a prevention of lunacy and a warning to others not to become lunatics. That was because lunacy was then thought to be an affair of the soul and not considered in terms of abnormal brain metabolism. To-day, some people still thought flogging, imprisonment and hanging were the best cure for aggressive crimes and the most salutary warning to others not to commit such aggressive acts. Dr. Hill's work suggested that some of our conceptions on this point were as foolish as those we shuddered at in lunacy a hundred years ago. It was fortunate that just as we were learning to diagnose such cases, so we were also learning how to treat them by means of ordinary drugs so that their brains did not "fire-off" so readily with simple environmental stress.

Dr. Alfred Meyer: My interest in the anatomical aspects of emotional expression has been aroused by an observation made in the course of investigations into the pathology of the Wernicke syndrome. In this syndrome now recognized to be due to thiamine deficiency a progressive clinical symptomatology of confusional states, Korsakow psychosis, somnolence and coma is associated with histological lesions within the grey matter around the 3rd ventricle, aqueduct and 4th ventricle. The most severe lesion in typical cases is situated in the caudal part of the hypothalamus, especially in the mammillary body. In one of my cases the localization of the hypothalamic lesion was, however, different. In this case, the oldest and most severe damage was found in the anterior (supra-optic) part of the hypothalamus. The cytoarchitectonic structure of the middle (tuberal) portion was approximately normal, although special staining revealed calcification of small blood-vessels, and the caudal (mammillary) region showed only slight and recent cellular degeneration. The interesting point is that in this case the mental picture was also atypical. During the first four months, of the illness, elation, hyperkinesia, flight of ideas, grandiose delusions and a marked tendency to angry and rage-like responses dominated the symptomatology, whereas confusion and memory defect supervened later, and death occurred in terminal coma about six months after the onset. I am greatly indebted to Dr. Lilly, superintendent of Cane Hill Hospital, for the clinical data of the case.

Manic-like syndromes as a result of hypothalamic lesions have recently attracted some attention. As the lesion is usually a tumour or a cyst in or near the hypothalamic area, a precise localization is, thus, difficult or impossible. My own case shows the essential clinico-pathological relations with an almost experimental clarity.

Bard, in his famous experiments, has demonstrated that sham rage in animals is due to activation of the undamaged caudal part of the hypothalamus. In his animals, the activation was brought about by extensive decortication often including the removal of the anterior hypothalamus; Fulton and Ingraham observed sham rage after bilateral lesions just in front of the chiasma, while Ranson and his collaborators produced the same results by damage to the anterolateral hypothalamic area. It is easily seen that the localization of the lesions in both instances is similar to that in my case.

The most plausible explanation is that the lesion in the rostral part of the hypothalamus interferes with inhibitory impulses coming from higher centres, particularly the frontal lobe. In this regard, the recent work of Spiegel, Miller and Oppenheimer has supplied further important experimental data. They produced rage in carnivores if the frontal lesion involved the parolfactory nuclei. It is of geat interest that a similar rage reaction occurred after bilateral ablation of the hippocampal region and the amygdaloid nuclei, while, as Papez pointed out, lesion of the anterior part of the cingular gyrus (anterior limbic region) has the opposite effect causing lack of emotional response, drowsiness, stupor and twilight states. The significance of these experimental results is seen, if the anatomical connexions of the hypothalamus are taken into consideration. The hypo-thalamus is linked with the parolfactory nuclei by the medial fore-brain bundle, with the prefrontal cortex via the dorsomedial nucleus of the thalamus, and with other parts of the frontal lobe via subthalamic and septal nuclei. The mammillary body maintains, through the anterior thalamic nucleus, connexions with the cingular gyrus, and the hippocampal region sends fibres via the fornix system to the septum pellucidum and to the mammillary body. There are also connexions with centres in the brain-stem and the pituitary. There is, thus, in the words of Papez, a well-interconnected cerebral mechanism involving the hypothalamus, parts of the frontal lobe, thalamic nuclei, cingular cortex, hippocampus and amygdaloid nuclei, whose function appears to be to elaborate and participate in emotional expression. All these centres are situated near the mid-line and they are commonly regarded as part of the rhinencephalon, although it is now proved that some of them do not serve olfactory function. The anterior limbic region and the Ammon's horn display their highest cytoarchitectonic differentiation in the human brain, although, in man, olfactory function is much reduced. In cases of arhinencephaly in which olfactory bulbs and tracts and cortical centres are absent, the pyramidal cortex of the Ammon's horn is not involved. It is also interesting that the cingular cortex has been regarded by Economo and Koskinas, more than fifteen years ago, as the cortical representation of the sympathetic system. There is on the other hand evidence that the parolfactory nuclei and the amygdaloid nuclei still serve olfactory function in man and for this reason may not have the same importance in the control of emotional expression as they have in macrosmatic species.

The difficulty of application of experimental results to the human brain will be gradually overcome by cytoarchitectonic studies, experimental research on a broad phylogenetic scale and, by patient collection of relevant data from human pathological material. I cannot go into detail but I should like to mention that we may have underrated the significance of the Ammon's horn sclerosis as a substrate of the emotional and personality changes in epileptics. Electroencephalography will be of the greatest help and, for a long time to come, it probably will be one of the principal methods available for localization of the subtle and reversible emotional phenomena in the field of so-called functional psychoses in which present histological methods are not likely to succeed. It provides some satisfaction to the anatomist, that with the introduction of this new method, anatomico-pathological data patiently collected by many workers become significant and some of the "silent" regions of the brain begin to speak, although, naturally, their language is still inarticulate and obscure in many ways.

A full account of my own case, the problems arising from it, and the literature will be given in a subsequent paper now being prepared for publication.

Section of Laryngology

President—W. M. MOLLISON, M.Ch.

[*March* 3, 1944]

DISCUSSION ON THE TREATMENT OF CARCINOMA OF THE ŒSOPHAGUS

Hermon Taylor, on opening the discussion, paid a tribute to the work of Professor Grey Turner who had fostered interest in the subject of carcinoma of the œsophagus more than any other surgeon in the country. The disease was of fairly common occurrence; the statistics of the Registrar-General included 1,703 male and 716 female deaths from this cause in 1937. Nevertheless the tumour was of relatively low malignancy, the rapid deterioration of patients being due to the œsophageal obstruction rather than to malignant cachexia. Dysphagia was unfortunately rather a late symptom and medical men should be on the watch for any complaint of aching or burning pain in the chest or throat associated with a tendency to regurgitation after meals. Such symptoms should always be investigated now that the modern operation of œsophagectomy was meeting with success in early cases of this disease. A less pessimistic and more vigorous attitude to this form of cancer was now indicated.

Radiotherapy by radium or X-rays had been disappointing by reason of inapplicability or of damage to vital organs, and though methods were improving the condition was essentially a surgical problem.

Discussing palliative methods, Mr. Hermon Taylor condemned gastrostomy as the fistula was distressing and saliva still had to be expectorated. He preferred methods directed to the restoration of swallowing, though these were more dangerous. Souttar's tube was often satisfactory and the endoscopic insertion of radon seeds was a good way of restoring the lumen by destroying the centre of the growth. Nevertheless palliation gave a poor measure of life and comfort and every risk should be taken to remove a growth that was operable.

The development of œsophagectomy for thoracic carcinoma was traced from the early part of this century. A great change had come about in the last decade whereby the development of anæsthetic methods, transfusion, and chemotherapy had largely removed the danger from an open pneumothorax on the operating table. Lilienthal's posterior mediastinal approach and Grey Turner's abdomino-cervical operation were both designed to avoid opening the pleural cavity and were therefore now of historical interest only. Sauerbruch's operation of endothoracic œsophago-gastrostomy after mobilizing the stomach up through the diaphragm had come into its own with the removal of the risk of thoracotomy. The Japanese Ohsawa had first successfully performed this operation ten years ago and since then it had become almost standardized for growths of the lower œsophagus.

Growths at a higher level were a more difficult anatomical problem. Although the facilitation of the transpleural approach had allowed Torek's operation of œsophageal resection with cervical œsophagostomy and abdominal gastrostomy to be successfully performed many times of late, little improvement in method had been found beyond making a skin tube between the fistulæ. This was not a satisfactory position; either the patient is left with two sore and troublesome fistulæ, or he has to undergo a series of

operations for the construction of a skin tube between them when he has already undergone a big operation and may yet develop metastases, with no promise that the tube itself will be satisfactory.

The speaker had therefore experimented with an operation which if successful would restore the continuity of the alimentary canal at one stage like the endothoracic method of Sauerbruch. Briefly it consisted in resecting the affected part of the œsophagus with immediate subcutaneous anastomosis *outside* the thorax. This was made possible by dislodging the stomach from beneath the diaphragm and drawing it high up in front of the sternum, immediately beneath the skin, where it reached easily, and could be at once anastomosed to, the upper portion of the œsophagus.

The technique of the operation was described elsewhere, but its performance in three cases had demonstrated its feasibility, although there was much to be learned in its further development. In the first two cases the growth was exposed and removed through a right thoracotomy; both these patients were frail subjects, but neither succumbed to the strain of the operation. One of them, a woman of 61, who was demonstrated at a recent meeting of the Clinical Section (*Proc. R. Soc Med.*, 1943, 37, 38), was now living at home, taking soft foods by mouth. The other, a man of 60, died of a persistent empyema eight months after operation, at which time there was no recurrence of the growth. In the case of the woman, infection of the suture line unfortunately prevented primary union of the anastomosis and a short indwelling tube was required to lie across the resulting fistula. She managed this tube entirely without assistance and was so well content with it that she did not wish for any operative closure of the fistula at that time.

The third case was a man with extensive carcinoma of the cardia and fundus of the stomach extending up the œsophagus. The operation was performed through a left thoracotomy and the proximal half of the stomach was removed as well as the lower third of the œsophagus. Nevertheless it was still possible to arrange a presternal anastomosis. Unfortunately a small tear in the opposite pleura led to an unsuspected partial pneumothorax of the right chest during the operation, which produced a degree of anoxæmia and circulatory collapse from which the patient could not be rallied and he died a short time after the operation.

None of the three cases was therefore quite straightforward but it would seem that in favourable circumstances the operation offered the following advantages: A mid-œsophageal growth could be removed and natural swallowing restored at a single operation, if primary union were achieved. No skin tubes were required. Leakage of the anastomosis was not fatal. If leakage did occur the fistula which resulted was easily bridged by a short indwelling tube. It could later be closed by a further adjustment of the stomach upwards without resorting to skin flaps. In the event of a very wide resection of growth, a gap could be deliberately left between the divided ends and bridged in this way by a tube—a procedure which would not be possible with the endothoracic method.

By postponing the mobilization of the stomach the operation could be performed in two stages with benefit in the case of a feeble patient. It could be performed from the left side as well as the right and was applicable to growths of the lower œsophagus and cardia. It could therefore be adopted in the latter type of case if for any reason an endothoracic anastomosis could not be obtained. The new gastro-œsophageal region would lie permanently beneath the skin. Here it could be manipulated if any obstruction should occur, it could be controlled if regurgitation were troublesome and it could be palpated periodically for recurrence of growth which would then be easily accessible to further treatment by surgery or by X-rays. (*Précis*)

W. M. Levitt: In December 1933 I showed to this Section seven of a series of eight cases of carcinoma of the œsophagus treated during the previous nine months by a strip-field method of deep X-ray therapy (*Proceedings*, 27, 368). All had had a high degree of œsophageal obstruction and all seven patients were able to swallow quite easily.

Skiagrams of seven primarily successful cases were shown, and in all seven, radiographic evidence of the disease had disappeared. In all, eight cases had been treated by this method up to the time of the communication but the eighth had died of an empyema before treatment could be completed. It was, of course, not to be expected that all these patients would be cured, but at least it seemed reasonable to hope that one or two of them at any rate, would survive for a long time. However, I now know that carcinoma of the œsophagus is still incurable. Remarkable palliation can be achieved by radiotherapy in selected cases but without such careful selection the price paid by the patient for a brief palliation can be too high.

Experience gained over the past twenty years has taught me to recognize the cases which should definitely be refused for radiotherapy, and if one accepts only cases which have been carefully selected I believe that the palliative value of X-ray therapy is considerable.

The subsequent history of these seven patients was as follows: Five of them sustained, as a result of their irradiation, such damage to pulmonary tissue that their deaths were ultimately determined by this, and not by their growths. In these cases, from six weeks to four months after treatment, the patients, while still swallowing well, began to complain of ·dyspnœa. The most careful clinical and radiographic examination failed at the beginning to reveal any cause for this dyspnœa. There was no cough and no other symptoms. Gradually the dyspnœa became worse until eventually the patient could only speak a few words without pausing for breath. By this time a diffuse fine fibrosis was observable in the skiagrams in the neighbourhood of the lung roots and the fibrosis gradually spread. Four of the six patients succumbed within a few months to acute infections which would probably have meant no more than an ordinary cold, had it not been for the lung damage. ·One patient, a woman with a middle-third growth, lived for nearly three years and then died of cardiac failure with generalized œdema and effusion into all the serous cavities. At autopsy no trace of carcinoma could be found in her body but a condition of brown atrophy was shown in the heart muscle which was attributed to the X-ray treatment. The seventh patient remained well for close on five years although the œsophagus had to be dilated from time to time for a fibrous stricture. He then got a recurrence which was treated without benefit and he died of his disease. This patient had no pulmonary symptoms throughout. The growth was in the upper third.

Modifications of the original method were then made in the direction of narrowing the beams still further and wherever possible reducing their number. It was found, however, that every attempt to reduce the width of the beam and thereby the size of the periœsophageal shell of tissue irradiated, was followed by a reduction in the proportion of primary disappearances of the growth and a reduction in the duration of the palliation. In spite of ten years of fairly steady advance in radiotherapeutic technique, I do not think the position has improved very greatly except in the upper-third growths. It is true that improved machines, and especially the super-high voltage machines, have increased the depth efficiency of our techniques and have enabled us to obtain better dosage distribution in the neighbourhood of the œsophagus while restricting lateral spread. Moreover accurate methods of beam direction have been introduced and knowledge of dosage distribution has improved. All these advances enable us to secure a better degree of palliation without lung damage. It is, however, still impossible to reproduce results, by X-ray therapy alone, approaching those obtained in the original series without inflicting some injury on the lung.

In selecting cases for treatment it scarcely needs stressing that patients with marked cachexia or with secondary deposits, or patients with complications such as cardiac or pulmonary disease, should not be submitted to radiotherapy. The most important contra-indication to radiotherapy, however, is mediastinitis. This is the condition which results from the spread of sepsis, perhaps associated with actual spread of growth through the œsophageal wall with consequent infection of the mediastinum. There are two cardinal signs of this condition which should be widely known as they constitute an absolute contra-indication to radiotherapy. First substernal pain, sometimes described as "shooting through to the scapula". The second, and more important, is persistent tachycardia usually without pyrexia. This latter sign I first described in 1934, and ten years of further observation have confirmed that it is a reliable guide to the presence of mediastinitis. I can safely say that I have never known a case of carcinoma of the œsophagus exhibiting this sign of persistent tachycardia not made worse by radiotherapy. If substernal pain is not already present it very soon makes its appearance after the initiation of X-ray treatment. As the radiation dose mounts up so the pain becomes worse and it can become so severe that the patient may be driven to suicide. Therefore no case of carcinoma of the œsophagus with persistent tachycardia with or without substernal pain should be submitted to radiotherapy. No case of carcinoma of the œsophagus with severe substernal pain, even in the absence of tachycardia should be submitted to radiotherapy. Pain is not a result of X-ray therapy in carcinoma of the œsophagus except in the presence of mediastinitis.

We have next to consider the influence of the site of the growth on the result. By far the best results are obtained in the upper third of the œsophagus while the results in the lower third of the œsophagus are so bad as to make treatment not worth while. Many of them are really growths of the cardia of the stomach. It is possible that some cures

may even be obtained in the upper third. I have two cases which seem to be qualifying for inclusion under this term. The middle-third cases give intermediate results.

The type of growth itself is important. The growths that show fat, fleshy fungations into the lumen of the œsophagus, usually well demonstrated in the skiagram and easily seen by the œsophagoscope, do best. Usually these growths are associated with a considerable periœsophageal shadow and they require treatment with rather wider fields although dosage need not be so high as to place the lung in danger of injury. First-class palliation can be obtained in these cases for a time which may vary from a few months to a couple of years or more.

To sum up, cases which should be excluded are those with signs of mediastinitis, pulmonary extension, secondary deposits and those with growth in the lower third. In the absence of the first contra-indication, every case showing large fleshy fungations is worth treating.

We must also remember that, as we have seen, with suitable dosage and distribution of radiations to the œsophagus and disregarding the lung, a very remarkable percentage of primary regressions can be obtained. The problem is largely one of dosage and dosage distribution. It is therefore pertinent to inquire whether, by judicious combination of X-rays with intracavitary radium, a sufficient dosage and a suitable dosage distribution would be obtained without undue lung exposure. I had just embarked in 1939 on a combined method of treatment when the outbreak of war cut short this work. If there is to be any hope of real cure of carcinoma of the œsophagus from radiotherapy, I think it must come on these lines, although it is *possible* that the further development of supervoltage therapy may contribute to solving our problem.

G. H. Steele: The outlook for a patient with carcinoma of the œsophagus is indeed gloomy because we are dealing in the majority of cases with a poor half-starved old man with a growth which has already spread to his vitals. Realizing this, we can merely try to relieve his dysphagia without attempting to cure his growth; in this category fall dilatation, intubation of the stricture, and gastrostomy. And when we boast of cures by other methods, do not let us forget the long periods of survival which occasionally follow such palliative measures alone.

We are dealing with a squamous epithelioma for which the obvious remedy is irradiation: but we have just heard Dr. Levitt's evaluation of the disappointing results of deep therapy; and there is remarkable unanimity among general practitioners who have to look after these cases subsequently as to how ill they are after intensive radiotherapy. As regards radium in the lumen, ten years ago the late Mr. Cleminson told this Section that he had treated 200 cases thus, and had come to the conclusion that they were better left alone. Some hope lies in the introduction of radon seeds through the œsophagoscope; and in spite of the inevitably hit-or-miss dosage due to difficulties in estimating the volume of growth to be irradiated and placement of the seeds, 50 to 70% of cases obtain great relief with a minimum of upset—a short anæsthetic, a minor operation, and a brief stay in hospital. Swallowing is restored for six months or so, at the end of which the patient dies rapidly instead of lingering for the whole of the time. Dr. Jobson and I have thus seeded 60 cases; there has been no operative mortality, the majority have been greatly improved, and we have had four three-year survivals. I operated upon a woman of 76 before the war; she is now 82 and swallowing quite well. At one time we tried seeding the lower end of the growth by retrograde transgastric œsophagoscopy as well, and although the distribution of the seeds was improved we came to the conclusion that the end-results were no better, while the patient was subjected to two operations instead of one.

The only justification for surgery is the poor cure-rate obtained otherwise. The ideal cancer operation is removal of the growth and glands in one block, but the application of this principle to the œsophagus bristles with difficulties. The thoracic œsophagus is inaccessible, and few of these poor-risk patients will stand a formidable thoracotomy. The growth spreads early to irremovable structures and secondary deposits are found from the neck to the abdomen: Churchill (1942) quotes figures showing that half of the growths at the lower end, and even one-third of the growths of the mid-œsophagus, metastasize below the diaphragm. However, as Grey Turner (1943) has said, removal of the œsophagus has been shown to be feasible: restoration of continuity is a more difficult problem. Direct anastomosis is obviously the most desirable course, but the œsophagus is poor material: it has no peritoneal coat, it is so friable that stitches cut out easily, and its septic contents are liable to infect pleura and mediastinum. The two ends can be

brought to the surface and joined by a tube of skin or intestine, but the majority of cases published in this country show that the unfortunate patient is subjected to many operations and is usually dead before the last one is completed. The openings can be joined by a rubber tube, but what a life!

Once the patient has been operated upon he has several stiff fences to surmount. If he does not die of shock in the first twenty-four hours; if he does not collapse or develop œdema of the lung in forty-eight hours, if his anastomosis does not leak at the end of four to five days, and if he does not develop an empyema in a week he has a good chance of survival.

I have two cases to report. Both had growths of the lower end of the œsophagus treated by left-sided transpleural resection; the diaphragm was opened, the stomach freed and brought up into the chest and anastomosed to the stump of the œsophagus. Both subsequently swallowed full meals normally; the first, a woman of 52, survived seven months and died of a recurrence; the second, a man of 72, was only operated upon three weeks ago, but he has left hospital perfectly well. He had relatively little dysphagia in spite of a big growth, which raises the question as to whether dilatation of the stricture might be preferable to gastrostomy as a means of pre-operative improvement.

Œsophagectomy now appears to be where gastrectomy was thirty to forty years ago: it has been shown to be feasible but the indications for its employment, except perhaps in growths of the lower end, are not yet fully established.

REFERENCES
CHURCHILL, E. D., and SWEET, R. H. (1942) *Ann. Surg.*, **115**, 897.
TURNER, G. GREY (1943) *Proc. R. Soc. Med.*, **37**, 39.

M. Lederman : The radium procedures available for the treatment of cancer of the œsophagus are: (1) External radiation by teleradium; (2) intracavitary treatment by radium bougie; (3) implantation of radon seeds. The technical method employed will depend on the part of the œsophagus affected and the purpose of treatment, whether cure or palliation.

Œsophageal cancer can be subdivided into pharyngo-œsophageal, mid- or thoraco-œsophageal and cardio-œsophageal tumours. This includes all neoplasms affecting the upper and lower ends of the œsophagus irrespective of site of origin. Whether an œsophageal tumour is primary in origin, or secondary to disease in the hypopharynx or cardia is of no great importance as far as planning of the radiation fields is concerned.

Pharyngo-œsophageal tumours.—Included in this group are tumours which are either limited to the cervical œsophagus or affect both this structure and the hypopharynx. These tumours are eminently suitable for teleradium treatment provided they do not extend below the 1st dorsal vertebra, *as once the upper thoracic aperture is passed the tumour becomes too deeply situated for efficient radiation by teleradium,* and high voltage X-ray therapy is indicated. High voltage X-ray therapy can, of course, be used as an alternative to teleradium for all cases, but the latter method has certain advantages of a technical, biological and physical nature.

Mid- or thoraco-œsophageal tumours.—There are two methods of radium treatment: A. Treatment by radium bougie; B. Treatment by radon implantation.

Because of the depth of the thoracic œsophagus below the surface teleradium treatment with present-day apparatus is not a satisfactory or economic alternative to high voltage X-ray therapy.

A. *Radium bougie.*—When treatment by radium bougie is undertaken a meticulous technique is essential. The chief features of the technique used at the Royal Cancer Hospital are as follows: (1) Accurate localization of the tumour: (*a*) Distance of upper edge of tumour from the upper incisor teeth obtained by œsophagoscopy; (*b*) length of the tumour. Information obtained by œsophagoscopy or X-rays. The length of œsophagus irradiated should be such as to include a wide margin of normal tissue above and below the tumour.

(2) The lumen of the œsophagus should be wide enough to take at least a No. 28 French œsophageal catheter. In some cases gradual preliminary dilatation of the œsophagus may be necessary. The *greater the diameter* of the catheter the better is the distribution of the radiation in the tumour. The size most commonly employed is a No. 30 French.

(3) Irrespective of the site of the primary growth the bougie must fill the whole length of the œsophagus. A short catheter or radium mounted on a Symonds' tube are unsatisfactory because they tend to be displaced upwards and it is difficult to be certain of their exact position during treatment.

(4) The radium tubes used have a linear density of 10 mg./cm. with an active length of 25 mm. and an overall length of 35 mm. Each is placed in a brass container 44 mm. long, and the total filtration is 1 mm. Pt equivalent. Tubes of higher linear density tend to give too intense a radiation, whilst tubes of lower linear density mean undue prolongation of treatment time. The bougie itself acts as a secondary filter.

(5) The containers should always be inserted so that the lowest appears at the catheter eyelet, which is filled in with wax before treatment is begun. By having the containers extending in tandem upwards from the lowest fixed portion of the catheter, a stable position is maintained. In order to fulfil this condition for all cases the lower part of the catheter may be occupied by empty containers when treating tumours of the upper part of the thoracic œsophagus.

(6) Secure anchorage of the bougie by tapes passing above and below the ears, coupled with vigilant nursing and observation are vital if the bougie is to remain in the selected position. X-ray examination after the first insertion should be performed as a routine.

(7) A divided dose method of treatment is employed. The bougie is inserted on alternate days and, using 25 mg. tubes, the total treatment time is sixty hours spread over fifteen days. By prolonging the treatment time, using relatively low radium content tubes, and employing the "shift" method to be described below, localized zones of intense radiation with consequent massive tumour necrosis are avoided.

(8) If the radiation field produced by a bougie constructed in this manner is examined, it is found that the radiation tends to be concentrated in zones in proximity to the radium-containing part of the tube, the inactive ends of the tubes and the ends of their cylindrical containers producing gaps where little radiation is given. The œsophagus is not a rigid, immobile structure and a certain amount of movement of its walls, partly inherent and partly transmitted, occurs. It is, however, both hazardous and unscientific to rely upon the vagaries of such movement to even out these differences in dose. The regions of under-dosage beneath the inactive portions of the radium container can be eliminated by arranging for a shift equal to half the length of one radium container, i.e. 22 mm. Deliberate steps are therefore taken for alternate treatments to be given in one of two different bougie positions. The shift not only eliminates the gaps but it also reduces the dose at the surface of the tumour from 20,000 r to 12,000 r with only a slight reduction in dose to points further away from the bougie.

B. *Radon seed implantation.*—Radon seeds can be used by insertion either through an œsophagoscope, or after transpleural exposure of the œsophagus. The disadvantages of these methods are that: It is impossible to insert radon seeds with the accuracy necessary for efficient irradiation of the whole tumour, and, moreover, the risks of perforation are not inconsiderable; it is doubtful if the risks associated with the operative procedure are justified for what can only be a palliative method.

Cardio-œsophageal tumours.—The abdominal œsophagus is usually affected secondarily by spread from an adjacent tumour of the cardiac end of the stomach. These cases are unsuitable for treatment by teleradium because of their depth below the surface, and a radium bougie cannot effectively deliver an adequate dose to the gastric part of the tumour; high voltage X-ray therapy, however, can be used.

Since 1936 a certain number of these cases have been treated at the Royal Cancer Hospital by the implantation of radon seeds after laparotomy. It has been found very difficult to devise accurate methods of distribution of the radon seeds. The radiographic appearances after a barium meal are of little assistance when attempting to assess the exact site and volume of the tissue affected by neoplasm for purposes of dose estimation. Again even after laparotomy these extensive, rather inaccessible tumours do not lend themselves to simple geometrical methods of radon seed distribution. As a routine we employ a maximum of 60 mc. of radon distributed as evenly as possible throughout the tumour tissue, in the form of seeds 6 mm. long, 0·3 mm. Pt filter and 2 mc. content. The seeds are inserted into the tumour substance via the serous surface and penetration into the lumen of the stomach is avoided. The risks of peritonitis following this procedure are small. Although the seeds are left in permanently, about 10 to 15% find their way into the bowel and are usually passed without incident. This method can obviously only be recommended as a last resort.

Results of radium treatment.—Out of a total of 15 cases of pharyngo-œsophageal tumours, three have been living symptom-free for a year, and one has developed metastases within that time; four died from intercurrent disease within four years, one from distant metastases in less than two years, and six died of their disease within one year. Although these results are not very striking, five of the cases died without any evidence of disease

in the treated area. Out of a total of 15 cases, 7 had lymph node metastases, 4 of which disappeared after treatment with recurrence in 1. There was primary healing in 12 cases with local recurrence in 2 cases.

In 38 cases of mid-œsophageal tumours 33 were treated by radium bougie and 5 by radon seeds. One survived two and a half years; the others died within six months.

In 15 cases of cardio-œsophageal tumours there were 2 post-operative deaths. Of the "useful" survivals on whom no gastrostomy had been performed there was one five-year survival, a patient under the care of Mr. R. C. B. Ledlie. Unfortunately there is no histological confirmation. One died of the disease in nineteen months and 3 died of the disease in six months.

COMMENTS

The best results yet obtained in the treatment of carcinoma of the œsophagus were those obtained by Guisez using a radium bougie. Unfortunately nobody seems to have been able to equal, much less emulate, his results. Of 270 cases treated by Guisez 11 survived more than three years, 12 survived over eighteen months, and 4 died of inter-current disease.

We have only had two survivals of appreciable length of time. One patient not included in this series was treated by Mr. Lawrence Abel in 1927 and died of intercurrent disease eleven years afterwards. The longest survival in this series is two and a half years.

No statistical table, however, can give any true picture of the palliative value of the bougie. The rapidity with which symptoms are relieved and the avoidance of gastrostomy are of incalculable value to the patient.

The treatment of cardio-œsophageal tumours by laparotomy and insertion of radon seeds does seem a worth-while procedure in an otherwise hopeless case.

Lieut.-Colonel W. L. Harnett, Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign, brought forward statistics of the results of treatment of carcinoma of the œsophagus collected by the Committee. Out of 15,200 cases of cancer registered during the seventeen months from April 1, 1938, to September 3, 1939, when the registration of new cases ceased, there were 470 cases of carcinoma of the œsophagus, about 3% of all cancer cases, approximately the same percentage as the Registrar-General's figures for England and Wales. There were 397 males and 76 females, a ratio of 5 males to 1 female, the same proportion as Vinson found in a study of 1,000 cases at the Mayo Clinic. The mean age of the males was $64 \cdot 67 \pm 0 \cdot 43$ years and of the females $61 \pm 1 \cdot 30$ years, the difference of the means $3 \cdot 03 \pm 1 \cdot 37$ being probably statistically significant.

Of these 470 cases, metastases in lymph nodes were recognizable clinically *in 80 cases* and distant metastases in 44, leaving 346 cases in which the disease, judged by clinical findings, was still local.

Methods of treatment used in these 470 cases were: Surgical, 205 cases; radium, 43 cases; X-rays, 139 cases. 105 cases received no treatment and 22 cases refused or abandoned treatment.

The thorax was explored in 17 cases and œsophagectomy was performed in 5 of these, all of which were operation fatalities. The operation mortality of thoracic exploration alone was 58·3%. Only 6 of the patients were alive at the end of the third year and in only one of these was the diagnosis based on a biopsy. The average duration was $9 \cdot 31 \pm 0 \cdot 31$ months. To assess the results of treatment it is necessary to allow for the varying expectation of life in groups of patients of either sex and of different ages and to calculate the ratio in each group between the *actual* duration of survival over a 3-year period of observation and the *expected* duration in a similarly constituted group of the general population. Calculated in this way it was found that cases treated by implantation of radon seeds had their expectation of life lengthened by two months

(4) The radium tubes used have a linear density of 10 mg./cm. with an active length of 25 mm. and an overall length of 35 mm. Each is placed in a brass container 44 mm. long, and the total filtration is 1 mm. Pt equivalent. Tubes of higher linear density tend to give too intense a radiation, whilst tubes of lower linear density mean undue prolongation of treatment time. The bougie itself acts as a secondary filter.

(5) The containers should always be inserted so that the lowest appears at the catheter eyelet, which is filled in with wax before treatment is begun. By having the containers extending in tandem upwards from the lowest fixed portion of the catheter, a stable position is maintained. In order to fulfil this condition for all cases the lower part of the catheter may be occupied by empty containers when treating tumours of the upper part of the thoracic œsophagus.

(6) Secure anchorage of the bougie by tapes passing above and below the ears, coupled with vigilant nursing and observation are vital if the bougie is to remain in the selected position. X-ray examination after the first insertion should be performed as a routine.

(7) A divided dose method of treatment is employed. The bougie is inserted on alternate days and, using 25 mg. tubes, the total treatment time is sixty hours spread over fifteen days. By prolonging the treatment time, using relatively low radium content tubes, and employing the "shift" method to be described below, localized zones of intense radiation with consequent massive tumour necrosis are avoided.

(8) If the radiation field produced by a bougie constructed in this manner is examined, it is found that the radiation tends to be concentrated in zones in proximity to the radium-containing part of the tube, the inactive ends of the tubes and the ends of their cylindrical containers producing gaps where little radiation is given. The œsophagus is not a rigid, immobile structure and a certain amount of movement of its walls, partly inherent and partly transmitted, occurs. It is, however, both hazardous and unscientific to rely upon the vagaries of such movement to even out these differences in dose. The regions of under-dosage beneath the inactive portions of the radium container can be eliminated by arranging for a shift equal to half the length of one radium container, i.e. 22 mm. Deliberate steps are therefore taken for alternate treatments to be given in one of two different bougie positions. The shift not only eliminates the gaps but it also reduces the dose at the surface of the tumour from 20,000 r to 12,000 r with only a slight reduction in dose to points further away from the bougie.

B. *Radon seed implantation.*—Radon seeds can be used by insertion either through an œsophagoscope, or after transpleural exposure of the œsophagus. The disadvantages of these methods are that: It is impossible to insert radon seeds with the accuracy necessary for efficient irradiation of the whole tumour, and, moreover, the risks of perforation are not inconsiderable; it is doubtful if the risks associated with the operative procedure are justified for what can only be a palliative method.

Cardio-œsophageal tumours.—The abdominal œsophagus is usually affected secondarily by spread from an adjacent tumour of the cardiac end of the stomach. These cases are unsuitable for treatment by teleradium because of their depth below the surface, and a radium bougie cannot effectively deliver an adequate dose to the gastric part of the tumour; high voltage X-ray therapy, however, can be used.

Since 1936 a certain number of these cases have been treated at the Royal Cancer Hospital by the implantation of radon seeds after laparotomy. It has been found very difficult to devise accurate methods of distribution of the radon seeds. The radiographic appearances after a barium meal are of little assistance when attempting to assess the exact site and volume of the tissue affected by neoplasm for purposes of dose estimation. Again even after laparotomy these extensive, rather inaccessible tumours do not lend themselves to simple geometrical methods of radon seed distribution. As a routine we employ a maximum of 60 mc. of radon distributed as evenly as possible throughout the tumour tissue, in the form of seeds 6 mm. long, 0·3 mm. Pt filter and 2 mc. content. The seeds are inserted into the tumour substance via the serous surface and penetration into the lumen of the stomach is avoided. The risks of peritonitis following this procedure are small. Although the seeds are left in permanently, about 10 to 15% find their way into the bowel and are usually passed without incident. This method can obviously only be recommended as a last resort.

Results of radium treatment.—Out of a total of 15 cases of pharyngo-œsophageal tumours, three have been living symptom-free for a year, and one has developed metastases within that time; four died from intercurrent disease within four years, one from distant metastases in less than two years, and six died of their disease within one year. Although these results are not very striking, five of the cases died without any evidence of disease

anticipated what would happen and accidents seldom occurred. The patient suffered very little disturbance. Seeds in the silk tube should be removed after ten days but catgut-coupled seeds should be left in position.

This was a method which could be considered in comparison with deep X-ray therapy as being very brief and with no effect on the lungs nor upset to the patient, who did not know that he had had more than a simple œsophageal examination.

A. Tudor Edwards said that some years ago he had carried out operations on 8 patients, 2 of whom were operable. In both cases it was possible to remove the growth. One was a woman of 60 who made a temporary recovery but died a month later from a purulent pneumonia. The second, a woman of 58, was shown to the Section in 1935 (*Proceedings*, 29, 188). She had almost a complete resection with the small portion of the upper œsophagus brought out of the neck and later connected with a rubber tube to the gastrostomy. She was the first patient in this country to be operated on by the transpleural method with the removal of the œsophagus. She died of recurrence seven months later.

In 1940 he had 7 cases, 3 of which were operable. One patient had a growth about 4 in. from the lower end and was treated by radical procedure, bringing out the upper œsophagus on to the chest. The operation was performed three years ago and the patient was still alive and free from symptoms. She had carried on with a tube. The question of a rubber tube was a question of the patient's persistence. Some people would get comfortable because they meant to do so and others would determine from the beginning that they would not be comfortable. He had left this patient alone and had not tried to carry out reconstruction. Skin tube reconstructions were very unsatisfactory. They should not be attempted too early. Many cases of successful resection of the œsophagus had died from pneumonia following the attempts of reformation of a gastric tube or skin tube for anastomosis. One should wait a long time before doing that.

At a recent meeting of the Society of Chest Surgeons nearly all those who had done partial resections of the œsophagus reported that fistulas occurred where they tried to reform skin tubes. A case operated on by Professor Grey Turner, after holding for a short time, had a fistula which was present until the man died.

Other attempts had been made to use tubes made from the stomach which were very difficult indeed to anastomose to skin satisfactorily and almost invariably leaked. The other method was to use the small intestine which did apparently form a satisfactory juncture with the œsophagus above and the stomach below, but one of the surgeons who had carried out three of these operations reported various disasters, one being the formation of a gastric ulcer where the small intestine was attached to the stomach, another developed a volvulus and the third had a very odd accident: the tube was attached the wrong way round and everything which was swallowed was rejected. He had anastomosed the upper end of the small intestine to the stomach, the difficulty had been got over and the patient was still alive.

He had a patient about three months ago in whom he was able to bring up the stomach, after division of the vessels on the left side, above the aorta and he had subsequent X-ray pictures of the anastomosis lying on a level with the aortic arch. It struck him at the time that it was an ideal method to adopt, and it was interesting that he had heard since that Garlock, an American surgeon, had recently reported a patient in whom he had performed an anastomosis above that level.

Another surgical point was the necessity of doing a left-sided exploration because it was necessary to remove any affected glands on the lesser curvature of the stomach. In the case in which he had successfully removed the growth and a good deal of the œsophagus the patient had three or four palpable glands in the region of the cardia; one of these was the size of the small finger-nail and the others were very small, one of which contained a microscopic metastasis. In a carcinoma below the aortic arch it was essential to open the diaphragm to remove those glands and the right-sided approach was inadvisable from that point of view.

The whole question of surgical resection and anastomosis in the chest relied on one factor—lack of tension. It was remarkable how freely and easily the stomach would come up and how good an anastomosis one could obtain within the chest.

R. D. Owen said he would like the opinion of deep therapy experts. He had in mind those cases of the Paterson Brown Kelly syndrome who gave the history of a "small swallow" for many years. Some of these improved very much after simple dilatation.

whilst in a group of 102 cases treated by deep X-ray therapy the average period of survival was twelve months instead of nine. The use of intracavitary radium in 26 cases did not increase the duration of survival.

For statistics *see 19th Annual Rep., British Empire Cancer Campaign*, 1942, 65-73.

D. W. Smithers said that he found it hard to believe that surgery was the answer to the problem of the treatment of carcinoma of the œsophagus. The quality of the life of those few patients who did survive was by no means enviable, whereas a patient who survived after radiotherapy swallowed normally. With modern X-ray techniques based on an estimation of the volume distribution of the energy absorbed radiotherapy should achieve better results. He had treated over 100 cases with X-rays, 80 of them more than two years ago and had not seen a single case of fibrosis of the lung in spite of the fact that 20 of these patients had lived for one year or more. Three patients were alive and free from symptoms more than five years after treatment (one after seven years, one after five years and nine months, and one after five years and five months, two with microscopical confirmation of the diagnosis). Of 32 patients who completed treatment before the war 30 had marked relief of symptoms and 11 became symptom-free for varying periods of time. No complete follow-up had yet been possible for patients treated during 1940 and 1941, but 12 were known to have been symptom-free at one period, and one of these, at least, for more than two years.

X-ray treatment could deal with the local growth in a reasonable proportion of cases, but the majority died from perforation or distant metastases. In eleven post-mortem examinations on patients who completed treatment there was definite evidence of persistence or recurrence of local growth in only three. X-ray treatment offered a means of relieving symptoms in quite a good proportion of these patients and produced an occasional five-year "cure", in fact it offered many of these patients useful palliation and provided some hope of survival. The literature showed that a five-year survival had followed radiotherapy in a number of patients; he was able to find ten to set against the only two surgical successes (Torek and Garlock) of the past thirty years, and when one considered the amount of palliation produced he thought that the evidence was strongly in favour of radiotherapy as the treatment method of choice.

One possibility for the future lay in a combination of radium and X-ray treatment. The chief trouble with the insertion of a radium bougie into the œsophagus was that the high local dose and trauma increased the risk of perforation. If a much smaller dose was given with radium and if this was supplemented by external high-voltage X-rays, the position might be improved.

V. E. Negus said that if the patient were in good condition, even with small glands, he believed the method described by Mr. Trotter of excision was worth considering. It was possible by excising the upper end of the œsophagus and reconstructing it with a skin tube to restore swallowing and to give the patient a happy life for some time. If for any reason the growth was intruding into the mediastinum it might be unsuitable for operative treatment, and local implantation of radon seeds outside the œsophagus might be practicable.

In cases of carcinoma of the thoracic œsophagus he too had tried to use radium in containers as described by Dr. Lederman, but had found that the only method which gave satisfactory results was the implantation of radon seeds. One could put the radon seeds into the bottom of the growth as well as into the top by using a proper depth indicator. It was, however, rather a haphazard method and he found that the better way was to couple the seeds together with links of catgut; an alternative method was to put the radon seeds into a small tube of silk. One examined the growth and measured it by passing bougies through and then made up a series of columns or chains of seeds, four or five in each according to the length of the growth. They were introduced through a wide bore œsophagoscope which had on it an arm so arranged that it held the stylet in position after an introducer had been passed in with the chain of seeds inside it. It was possible with these columns of seeds to give a fairly even distribution, and they were mutually self-retaining. By this method it was impossible to cure a growth, because of the outward extension, but it was almost always possible to restore swallowing with very little discomfort to the patient; and although the patient's life was not prolonged it did allow him to swallow in a normal way not only food but, what was more important, saliva. These people died from perforation if the growth were in the region of the trachea or bronchi and death might be precipitated by the introduction of the seeds; but it only

Section of Urology

President—E. W. RICHES, M.C., M.S.

[*January 27, 1944*]

The Diagnosis and Treatment of Infections of the Male Genital Organs other than Tuberculosis and Gonorrhœa [*Abridged*]

By R. H. O. B. ROBINSON, F.R.C.S.

OUR outlook has been revolutionized by the introduction of the sulphonamides so that some of the conditions now to be considered may scarcely be met with in the future. This applies particularly to those conditions which are initiated by gonorrhœa or its misdirected treatment. Certain infections are strictly venereal in origin, such as infestation with *Trichomonas vaginalis*, whereas others may be so occasionally. Many instances of *Bacillus coli* infection appear to have been transmitted by sexual contact. Obviously there is a tendency for genital infections to involve the whole generative tract, but the lesion in one situation is often the predominant feature.

When we discuss orchitis and epididymitis it is unusual to find one without some degree of the other. The testis may be invaded via the blood-stream, or by direct extension from the epididymis. Blood-stream infections are due to mumps, typhoid and syphilis. The orchitis of mumps may be in rare instances the only manifestation of the disease. Its average incidence is 15% and it seldom occurs before puberty.

Typhoid orchitis is a very rare complication of the fever, and may occur in the convalescent period. The liability to suppuration is high. Other causes of mild hæmatogenous orchitis are influenza, smallpox, diphtheria and pyæmia. It is interesting to consider the possibility propounded by Barney that the testis is, like the kidney, an excretory organ for bacteria and their toxins.

The two common varieties of epididymitis, gonorrhœal and tuberculous, are excluded from this paper but non-specific epididymitis is just as common as the more widely recognized types. Its ætiology is varied, but infection, trauma and congestion are all factors. Infection may spread from the posterior urethra or be metastatic. The common organisms isolated are the *Bacillus coli*, staphylococci and streptococci—although some authorities prefer to regard *B. coli* infections as an example of a specific epididymitis. A possible cause of infection is the forcing back of urine into the ejaculatory ducts during violent exercise with a full bladder. In many cases sterile pus is found in the urine, owing presumably to the causative organisms having died off naturally or as the result of treatment. In such cases exhaustive tests fail to reveal any evidence of tuberculosis. Metastatic infections are seen in influenza and meningitis. Trauma, by producing interstitial hæmorrhage or thrombosis, may give rise to a condition clinically indistinguishable from epididymitis, while congestion, as in the so-called erotic epididymitis, may produce tenderness and swelling with considerable local discomfort.

To assess the frequency of non-specific epididymitis, an analysis of cases of epididymitis admitted to St. Thomas's Hospital (Robinson, 1943) showed that rather over 50% were of this type. The outstanding features were the chronicity, tendency to relapse and liability to confusion with tuberculosis.

Syphilitic infections chiefly affect the testis either as a diffuse sclerosis or as a localized gumma. It may also affect one epididymis, and I had to deal recently with a case of gumma of the epididymis. This is a recognized clinical entity and resembles non-specific epididymitis or neoplasm of the epididymis. If suspected, the diagnosis is con-

Others did not, and in these, on direct examination, one could see marked cricopharyngeal stenosis, with atrophic mucosa bleeding easily on being touched. One felt that this was definitely pre-cancerous and that sooner or later a post-cricoid carcinoma would be a certainty.

He would like to know whether teleradium or deep therapy would help in preventing the full cancerous manifestation.

N. S. Finzi said that he had had several cases in which there was improvement with radium; one case with a growth at the lower end of the œsophagus survived for six years and then died with a gastric ulcer. The post-mortem showed that the growth had been cured so that they could not absolutely generalize about never treating the lower end. There were occasionally cases which could be cured by radium therapy.

As regards intracavitary radium, he had experience of two cases which had died for no apparent reason. On post-mortem no reason for death could be found, so that there was a danger in intracavitary radium which had not been mentioned. Nevertheless he thought the solution was what Dr. Levitt had said, that the effect of intracavitary radium plus external radiation should be tried. It was possible that by this method results would be obtained which would not occur by using either treatment alone.

Hermon Taylor, in reply, said that the discussion had emphasized the necessity of obtaining microscopical proof of the diagnosis in all cases. The only five-year cures mentioned, one by Dr. Lederman and five from Dr. Harnett's statistical tables were cases without a biopsy and diagnosed on the radiological appearances only. Such cases should not be included in statistical figures as X-ray diagnosis could be misleading, for example in the case of simple ulcer at the cardia associated with congenital short œsophagus. Answering Dr. Smithers he stressed the fact that the modern technique of œsophagectomy was a very recent development, methods were improving annually, and comparison of results between surgery and radiology should not be based on figures older than five or six years. The present trend indicated that surgery offered more scope than radiotherapy.

W. M. Levitt, in reply, said that some precancerous conditions were radiosensitive, others were not. He would not be prepared to treat this condition on the lines of a carcinoma of the œsophagus unless there were a definite carcinoma there.

In reply to Mr. Steele: The degree of illness inflicted on patients by radiotherapy was not great if the cases were carefully selected. Some of the patients had insisted on doing office work during their treatment. Mr. Negus would remember a patient who at the end of his treatment was going to his club and was able to swallow. But the cases must be carefully selected.

M. Lederman, in reply, said that practically all the cases he had shown had had a biopsy performed but the best cardio-œsophageal case had not had one. These latter cases were so hopeless that one was surprised when a good result was obtained.

Section of Urology

President—E. W. RICHES, M.C., M.S.

[January 27, 1944]

The Diagnosis and Treatment of Infections of the Male Genital Organs other than Tuberculosis and Gonorrhœa *[Abridged]*

By R. H. O. B. ROBINSON, F.R.C.S.

OUR outlook has been revolutionized by the introduction of the sulphonamides so that some of the conditions now to be considered may scarcely be met with in the future. This applies particularly to those conditions which are initiated by gonorrhœa or its misdirected treatment. Certain infections are strictly venereal in origin, such as infestation with *Trichomonas vaginalis*, whereas others may be so occasionally. Many instances of *Bacillus coli* infection appear to have been transmitted by sexual contact. Obviously there is a tendency for genital infections to involve the whole generative tract, but the lesion in one situation is often the predominant feature.

When we discuss orchitis and epididymitis it is unusual to find one without some degree of the other. The testis may be invaded via the blood-stream, or by direct extension from the epididymis. Blood-stream infections are due to mumps, typhoid and syphilis. The orchitis of mumps may be in rare instances the only manifestation of the disease. Its average incidence is 15% and it seldom occurs before puberty.

Typhoid orchitis is a very rare complication of the fever, and may occur in the con-valescent period. The liability to suppuration is high. Other causes of mild hæmato-genous orchitis are influenza, smallpox, diphtheria and pyæmia. It is interesting to consider the possibility propounded by Barney that the testis is, like the kidney, an excretory organ for bacteria and their toxins.

The two common varieties of epididymitis, gonorrhœal and tuberculous, are excluded from this paper but non-specific epididymitis is just as common as the more widely recognized types. Its ætiology is varied, but infection, trauma and congestion are all factors. Infection may spread from the posterior urethra or be metastatic. The common organisms isolated are the *Bacillus coli*, staphylococci and streptococci—although some authorities prefer to regard *B. coli* infections as an example of a specific epididymitis. A possible cause of infection is the forcing back of urine into the ejaculatory ducts during violent exercise with a full bladder. In many cases sterile pus is found in the urine, owing presumably to the causative organisms having died off naturally or as the result of treatment. In such cases exhaustive tests fail to reveal any evidence of tuberculosis. Metastatic infections are seen in influenza and meningitis. Trauma, by producing inter-stitial hæmorrhage or thrombosis, may give rise to a condition clinically indistinguishable from epididymitis, while congestion, as in the so-called erotic epididymitis, may produce tenderness and swelling with considerable local discomfort.

To assess the frequency of non-specific epididymitis, an analysis of cases of epididy-mitis admitted to St. Thomas's Hospital (Robinson, 1943) showed that rather over 50% were of this type. The outstanding features were the chronicity, tendency to relapse and liability to confusion with tuberculosis.

Syphilitic infections chiefly affect the testis either as a diffuse sclerosis or as a localized gumma. It may also affect one epididymis, and I had to deal recently with a case of gumma of the epididymis. This is a recognized clinical entity and resembles non-specific epididymitis or neoplasm of the epididymis. If suspected, the diagnosis is con-

firmed by serological tests and the clinical history. Iodides and mercury should produce resolution, but occasionally orchidectomy may be necessary.

A form of epididymitis due to blastomycosis has been described at the Mayo Clinic by Jacobson (1943) as part of a generalized blastomycotic infection of the genital tract, known in America as Gilchrist's disease. The local effects resemble very closely those due to tuberculosis.

Infections of the vas alone do not constitute a prominent surgical group.

It is interesting that, although epididymitis is reputed to follow prostatectomy in 10% of cases where the vas has not been divided, it is very much less common to meet with abscess formation and funiculitis round the stump of the divided vas. A curious condition has been described recently by Benjamin (1943) as vasitis nodosa, in which the clinical features are those of beading, clinically resembling tuberculosis. Microscopic examination reveals numerous diverticula in the walls of the vas, and the ætiology is obscure.

The seminal vesicles tend to harbour infection in much the same manner as the gall-bladder. In many instances the infection commences during an attack of gonorrhœa, but subsequently there is a mixed infection with other organisms, the effects of which are usually insidious rather than dramatic. The actual lesion may be fibroid thickening or an empyema of the vesicle, the so-called pus tube. Locally there may be symptoms of irritation of the base of the bladder and posterior urethra, very often associated with prostatitis. Naturally enough, a diagnosis of chronic prostatitis may be made and the more important lesion overlooked. In other cases chronic epididymitis may also be associated with vesiculitis, a definite indication for vasotomy or vasectomy. Metastatic lesions resulting from toxic absorption may be seen as arthritis, fasciitis or iritis. The condition is also particularly associated with a peculiar mental state of depression in which various sexual symptoms may occur. Hæmatospermia may also be noticed, but personally I have found that in the majority of instances of hæmatospermia as an isolated symptom, no demonstrable lesion can be found and the patient can be reassured. In vesiculitis the posterior urethroscope usually reveals very definite changes such as polyposis, congestion of the colliculus, and pus exuding from the ejaculatory ducts. The treatment consists in massage and diathermy with the passage of a Kollman dilator or large bougie. After massage, bladder lavage with preparations of silver is often beneficial. Where relapsing infection of the epididymis is present, vasotomy with irrigation of the vesicle with silver salts, as advocated by Belfield, is indicated. This appears to be the only way of vesicular medication, as catheterization of the ejaculatory ducts through an endoscope is not practicable in the majority of cases. In cases where the vesicle is merely a pus tube, vesiculectomy by perineal dissection is the only operation which is likely to produce permanent relief. This operation is one of considerable technical difficulty and, if carried out on both sides, is liable to be followed by impotence.

Vesiculitis is often present with chronic cystitis secondary to enlargement of the prostate. It may account for those cases which show a flare of local sepsis after prostatectomy, and particularly for those in which the urinary infection lingers on for months after the prostate has been removed. This was stressed by Thomson Walker, who elaborated transvesical vesiculectomy to deal with it. In the majority the condition appears to subside in due course—no doubt owing to the double effect of ligature of the vas stopping distension of the vesicle, and of efficient emptying of the bladder removing the infecting reservoir. One of the arguments to my mind against the Harris type of prostatectomy is that the posterior sutures are liable to interfere with the elimination of, even if not to produce, infection in the vesicle.

Infections of the prostate may be classified as acute or chronic, and in both instances can reach the gland from the urethra or the blood-stream. I have often seen dental infection as the causative lesion of an acute or persistent chronic prostatitis. Acute infection other than that due to the gonococcus is rare and is usually due to blood-borne infection. In neglected cases perineal suppuration with the development of a complicated fistula-in-ano may result.

Chronic prostatitis is usually the aftermath of gonorrhœal infection, secondary infecting organisms being found. This is important, as the individual is not usually liable to infect his partner and therefore can be spared the depressing psychological effects of apprehension. The condition is frequently associated with chronic vesiculitis, and shares with it the tendency to sexual neurasthenia. Other infective foci in the urinary tract and elsewhere in the body should be searched for and, if found, treated appropriately. As illustration, one might quote the *B. coli* infection of an abnormal kidney or apical dental infection.

Treatment consists in attention to the general health and well-being, and locally in prostatic massage, dilatation of the posterior urethra, instillation of silver preparations, and diathermy.

The role of massage is of considerable interest, as it presumably produces its greatest effect by stimulating circulatory exchanges in the gland and producing reflex secretion, rather than by possible evacuation of infected foci. At any rate, this last effect would be definitely dangerous in view of the risk of local spread of infection and systemic absorption, which we not infrequently see after too vigorous efforts on the part of the manipulator.

There are two end-results of chronic prostatitis that are of considerable interest and importance—namely prostatic calculi and prostatic bar. Calculi consist of deposits of phosphates and carbonates on corpora amylacea, and are found in the deeper parts of the gland at a distance from the urethra. They are invariably associated with sclerosis of the neck of the bladder and trigone, so that, as Swift Joly has pointed out, the prostate resembles a pie, the trigone forming the crust. Crepitus can very often be palpated on rectal examination, and the X-ray appearances are very typical, in some cases the individual lobes of the prostate being outlined. In many cases, calculi are discovered in the course of routine examination and are of no significance unless producing symptoms. Whatever method is used for their removal, should this be deemed necessary, must deal with associated contraction of the bladder neck. Personally, I prefer a suprapubic approach, using the diathermy knife.

Inflammatory bar at the bladder neck is one of the commoner causes of unsatisfactory micturition. In the prodromal stage a great deal can be done by treatment of the chronic prostatitis. In the later fibrous stage perurethral resection is indicated, but the inflammatory origin must be remembered and any reactivation of prostatitis following on operation treated energetically. All cases should be followed carefully and watched for fresh contracture.

Non-specific urethritis is not infrequently seen following chemical irritation, the result of prophylactic or contraceptive irrigations. It also occurs, as mentioned previously, in mumps, meningitis, infective fevers, *B. coli* and Trichomonas infestation. Incidentally, this last is an example proving that non-specific urethritis is often a symptom of an undetected chronic prostatitis. Pyogenic urethral infection is usually associated with the insertion of foreign bodies, and in my experience nothing is more productive of urethritis than the indwelling catheter. A catheter must provoke a discharge from the urethral mucosa, and provided that this can escape freely from the meatus no harm will result. If, however, the catheter is large enough to plug the external meatus tightly, or if the catheter is retained by some contrivance which encircles the penis entirely—thereby occluding the lumen of the urethra round the external surface of the catheter—the results may be catastrophic. If the unfortunate patient is the victim of a spinal lesion the effects are enhanced. Catheters of the Foley type have achieved an enormous advance and should be more widely appreciated. Pyogenic infection is often resistant to treatment in cases where long-standing urethral strictures are present. Urethrorrhœa should not be confounded with urethritis.

Stenosing balanoposthitis associated with phimosis I have found to be a fairly common cause of urinary difficulty in the elderly, the symptoms being usually loosely attributed to prostatism.

It is common to find a gross degree of meatal stricture in such cases, due to a secondary urethritis together with a filthy condition of the preputial sac. Circumcision is indicated, if necessary by a preliminary dorsal slit. A pyogenic infection under an irretractable prepuce may conceal a more sinister lesion.

Peyronie's disease, or indurative cavernositis, is a not uncommon and interesting condition of patchy fibrosis and calcification in the dorsal sheath of the corpus cavernosum, and often in the intercavernous septum. I have not been impressed by the results of radiotherapy in this condition, and as a rule, fortunately, it is not a cause of gross disability.

The virus of lymphogranuloma enters via the urethral mucosa, but does not as a rule produce any local lesion or manifestation other than some slight discharge, and probably escapes detection until the typical glandular involvement occurs. It is, of course, to all intents and purposes, unknown in a white population.

REFERENCES

BENJAMIN, J. A., ROBERTSON, J. D., and CHEETHAM, J. G. (1943) *J. Urol.*, 49, 575.
JACOBSON, C. E., Jr., and DOCKERTY, M. B. (1943) *J. Urol.*, 50, 237.
ROBINSON, R. H. O. B. (1943) *Proc. R. Soc. Med.*, 36, 325.

firmed by serological tests and the clinical history. Iodides and mercury should produce resolution, but occasionally orchidectomy may be necessary.

A form of epididymitis due to blastomycosis has been described at the Mayo Clinic by Jacobson (1943) as part of a generalized blastomycotic infection of the genital tract, known in America as Gilchrist's disease. The local effects resemble very closely those due to tuberculosis.

Infections of the vas alone do not constitute a prominent surgical group.

It is interesting that, although epididymitis is reputed to follow prostatectomy in 10% of cases where the vas has not been divided, it is very much less common to meet with abscess formation and funiculitis round the stump of the divided vas. A curious condition has been described recently by Benjamin (1943) as vasitis nodosa, in which the clinical features are those of beading, clinically resembling tuberculosis. Microscopic examination reveals numerous diverticula in the walls of the vas, and the ætiology is obscure.

The seminal vesicles tend to harbour infection in much the same manner as the gall-bladder. In many instances the infection commences during an attack of gonorrhœa, but subsequently there is a mixed infection with other organisms, the effects of which are usually insidious rather than dramatic. The actual lesion may be fibroid thickening or an empyema of the vesicle, the so-called pus tube. Locally there may be symptoms of irritation of the base of the bladder and posterior urethra, very often associated with prostatitis. Naturally enough, a diagnosis of chronic prostatitis may be made and the more important lesion overlooked. In other cases chronic epididymitis may also be associated with vesiculitis, a definite indication for vasotomy or vasectomy. Metastatic lesions resulting from toxic absorption may be seen as arthritis, fasciitis or iritis. The condition is also particularly associated with a peculiar mental state of depression in which various sexual symptoms may occur. Hæmatospermia may also be noticed, but personally I have found that in the majority of instances of hæmatospermia as an isolated symptom, no demonstrable lesion can be found and the patient can be reassured. In vesiculitis the posterior urethroscope usually reveals very definite changes such as polyposis, congestion of the colliculus, and pus exuding from the ejaculatory ducts. The treatment consists in massage and diathermy with the passage of a Kollman dilator or large bougie. After massage, bladder lavage with preparations of silver is often beneficial. Where relapsing infection of the epididymis is present, vasotomy with irrigation of the vesicle with silver salts, as advocated by Belfield, is indicated. This appears to be the only way of vesicular medication, as catheterization of the ejaculatory ducts through an endoscope is not practicable in the majority of cases. In cases where the vesicle is merely a pus tube, vesiculectomy by perineal dissection is the only operation which is likely to produce permanent relief. This operation is one of considerable technical difficulty and, if carried out on both sides, is liable to be followed by impotence.

Vesiculitis is often present with chronic cystitis secondary to enlargement of the prostate. It may account for those cases which show a flare of local sepsis after prostatectomy, and particularly for those in which the urinary infection lingers on for months after the prostate has been removed. This was stressed by Thomson Walker, who elaborated transvesical vesiculectomy to deal with it. In the majority the condition appears to subside in due course—no doubt owing to the double effect of ligature of the vas stopping distension of the vesicle, and of efficient emptying of the bladder removing the infecting reservoir. One of the arguments to my mind against the Harris type of prostatectomy is that the posterior sutures are liable to interfere with the elimination of, even if not to produce, infection in the vesicle.

Infections of the prostate may be classified as acute or chronic, and in both instances can reach the gland from the urethra or the blood-stream. I have often seen dental infection as the causative lesion of an acute or persistent chronic prostatitis. Acute infection other than that due to the gonococcus is rare and is usually due to blood-borne infection. In neglected cases perineal suppuration with the development of a complicated fistula-in-ano may result.

Chronic prostatitis is usually the aftermath of gonorrhœal infection, secondary infecting organisms being found. This is important, as the individual is not usually liable to infect his partner and therefore can be spared the depressing psychological effects of apprehension. The condition is frequently associated with chronic vesiculitis, and shares with it the tendency to sexual neurasthenia. Other infective foci in the urinary tract and elsewhere in the body should be searched for and, if found, treated appropriately. As illustration, one might quote the B. coli infection of an abnormal kidney or apical dental infection.

Treatment consists in attention to the general health and well-being, and locally in prostatic·massage, dilatation of the posterior urethra, instillation of silver preparations, and diathermy.

The role of massage is of considerable interest, as it presumably produces its greatest effect by stimulating circulatory exchanges in the gland and producing reflex secretion, rather than by possible evacuation of infected foci. At any rate, this last effect would be definitely dangerous in view of the risk of local spread of infection and systemic absorption, which we not infrequently see after too vigorous efforts on the part of the manipulator.

There are two end-results of chronic prostatitis that are of considerable interest and importance—namely prostatic calculi and prostatic bar. Calculi consist of deposits of phosphates and carbonates on corpora amylacea, and are found in the deeper parts of the gland at a distance from the urethra. They are invariably associated with sclerosis of the neck of the bladder and trigone, so that, as Swift Joly has pointed out, the prostate resembles a pie, the trigone forming the crust. Crepitus can very often be palpated on rectal examination, and the X-ray appearances are very typical, in some cases the individual lobes of the prostate being outlined. In many cases, calculi are discovered in the course of routine examination and are of no significance unless producing symptoms. Whatever method is used for their removal, should this be deemed necessary, must deal with associated contraction of the bladder neck. Personally, I prefer a suprapubic approach, using the diathermy knife.

Inflammatory bar at the bladder neck is one of the commoner causes of unsatisfactory micturition. In the prodromal stage a great deal can be done by treatment of the chronic prostatitis. In the later fibrous stage perurethral resection is indicated, but the inflammatory origin must be remembered and any reactivation of prostatitis following on operation treated energetically. All cases should be followed carefully and watched for fresh contracture.

Non-specific urethritis is not infrequently seen following chemical irritation, the result of prophylactic or contraceptive irrigations. It also occurs, as mentioned previously, in mumps, meningitis, infective fevers, *B. coli* and Trichomonas infestation. Incidentally, this last is an example proving that non-specific urethritis is often a symptom of an undetected chronic prostatitis. Pyogenic urethral infection is usually associated with the insertion of foreign bodies, and in my experience nothing is more productive of urethritis than the indwelling catheter. A catheter must provoke a discharge from the urethral mucosa, and provided that this can escape freely from the meatus no harm will result. If, however, the catheter is large enough to plug the external meatus tightly, or if the catheter is retained by some contrivance which encircles the penis entirely— thereby occluding the lumen of the urethra round the external surface of the catheter— the results may be catastrophic. If the unfortunate patient is the victim of a spinal lesion the effects are enhanced. Catheters of the Foley type have achieved an enormous advance and should be more widely appreciated. Pyogenic infection is often resistant to treatment in cases where long-standing urethral strictures are present. Urethrorrhœa should not be confounded with urethritis.

Stenosing balanoposthitis associated with phimosis I have found to be a fairly common cause of urinary difficulty in the elderly, the symptoms being usually loosely attributed to prostatism.

It is common to find a gross degree of meatal stricture in such cases, due to a secondary urethritis together with a filthy condition of the preputial sac. Circumcision is indicated, if necessary by a preliminary dorsal slit. A pyogenic infection under an irretractable prepuce may conceal a more sinister lesion.

Peyronie's disease, or indurative cavernositis, is a not uncommon and interesting condition of patchy fibrosis and calcification in the dorsal sheath of the corpus cavernosum, and often in the intercavernous septum. I have not been impressed by the results of radiotherapy in this condition, and as a rule, fortunately, it is not a cause of gross disability.

The virus of lymphogranuloma enters via the urethral mucosa, but does not as a rule produce any local lesion or manifestation other than some slight discharge, and probably escapes detection until the typical glandular involvement occurs. It is, of course, to all intents and purposes, unknown in a white population.

REFERENCES

BENJAMIN, J. A., ROBERTSON, J. D., and CHEETHAM, J. G. (1943) *J. Urol.*, 49, 575.
JACOBSON, C. E., Jr., and DOCKERTY, M. B. (1943) *J. Urol.*, 50, 237.
ROBINSON, R. H. O. B. (1943) *Proc. R. Soc. Med.*, 36, 325.

DISCUSSION ON ENURESIS

Mr. T. Twistington Higgins : Enuresis has been defined by Zappert (Meredith Campbell) as: "The involuntary and usually unconscious voiding of large amounts of urine, which occurs predominantly during sleep, in the absence of organic disease of the nervous or urological systems."

However, we cannot exclude "voluntary enuresis", i.e. the case of those children who, from some psychological aberration or, it may be, from degraded social custom, are deliberately dirty in their habits.

Again, it is generally agreed that we should not begin to speak of "enuresis" until a child is 3½ to 4 years old, but I think this needs some qualification.

The normal child should have acquired control of its bladder function long before this. A healthy infant, properly trained, should be dry after 18 months at the latest—many much earlier. Thereafter "accidental" mishaps should be rare events. If, in such an infant, there is frequent flooding, something is likely to be wrong. If this is not appreciated, a gross uropathy may well pass unrecognized in its early stages. Enuresis may be a prominent feature of certain rare diseases such as diabetes and hyperpiesia. Spina bifida occulta, when unassociated with other neurological signs, is a rare cause of enuresis, though this possibility should be borne in mind, particularly in the case of sacral defects.

Organic Disease of the Urological System

Approximately one case in ten of enuresis in children will be found to have some organic disorder of the urinary tract, so that a comprehensive clinical examination directed in particular to the urinary organs is necessary.

The urinary tract lesions to be expected are almost all due either to obstruction in the tract, or to infection, or to a combination of both. The history may at once provide suggestive evidence. If the wetting consists of the frequent and urgent voiding of small quantities of urine, especially if there is any associated pain, and possibly, febrile attacks, there is likely to be a urinary infection. Again, straining and difficulty in the act of micturition point to an obstruction, and much may be learned in such a case from having the child pass its urine under our observation.

Examination of the external genitals: (*a*) In the girl. Vulvovaginitis is the commonest lesion. It may only be slight and transient, but in my experience it is a frequent source of infection and enuresis. It is remarkable how frequently both are cured with its disappearance. The urethra should be inspected for signs of inflammation, malformation, &c.

(*b*) In the boy. The external meatus should be examined for contraction, ulceration or malformation. A glandular hypospadias is often unrecognized, and of course, with this deformity, contracture of the misplaced meatus is almost always the rule.

Phimosis: It is generally agreed to-day that phimosis is rarely, if ever, a cause of enuresis. In my view circumcision has no place in the treatment of enuresis. There is no operation in surgery performed with so much frequency yet with such little cause as that of circumcision.

Distended bladder and residual urine: If the bladder is distended then an effort should be made to estimate the residual urine. It only means passing a catheter after the child has voided as completely as possible. The presence of residual urine in any quantity means obstruction of some sort, and is, therefore, a valuable sign.

Urinary analysis: There should be a complete investigation of the urine, including culture.

If examination has revealed nothing abnormal, then the enuresis may be assumed to be "functional", and appropriate treatment adopted. If, after three months, there is no improvement, a complete urological investigation should be made when an organic cause may be revealed, such as:

Infections

Acute and subacute infections are readily recognized and treatment by drugs and diet is commonly successful. It is only when the infection is resistant, or when it recurs, when, therefore, some form of urinary obstruction is probably a complication, that a complete urological investigation is necessary to determine treatment. This may involve anything

from simple dilatation, to possible extirpation of a chronic, infected focus. Even when a urinary infection has been cleared there may be a sterile, clear urine, a normal bladder with perhaps a mild dilatation of one or both ureters, or of the renal pelvis, or even of the calices. This mild abnormality may be associated with the child's enuresis. We must picture the whole urinary duct as one co-ordinated neuromuscular mechanism, devised to ensure regular peristalsis, with proper filling and emptying of the reservoirs. This perfect arrangement is easily disturbed under the stress of inflammatory lesions, and irregular peristalsis and spasm induced. Indeed active degenerative changes in the wall of the duct may follow serious and lasting infections, leading to permanent dilatation (ureterectasis). Such disturbances—irritable peristalsis and spasm—may well persist for varying periods after the actual infection has disappeared, and even when they are only demonstrable in the upper tract, bladder irritability, and enuresis are thus explained.

All this is even more apparent in the bladder itself, where a cystitis which may have completely cleared up leaving a sterile urine, may nevertheless leave in its trail for a considerable period a degree of vesical irritability—which will determine an enuresis.

Such bladders frequently show an angry red hyperæmia of the area around the internal urinary meatus and adjacent part of the trigone, with perhaps a polypoid appearance—the commonly styled urethrotrigonitis. Like the primary cystitis which it probably follows, it is one of the commonest urological findings in girls with enuresis. Instillations of silver nitrate 1:500 are of use, and in some cases a touch or two with the diathermy electrode may benefit.

Obstructive Lesions

In boys it is the urethral obstructions which are important. The commonest, and happily also the simplest to deal with, is the contracted external urinary meatus. The posterior urethral lesions and bladder-neck obstructions form an important group, presenting much difficulty in diagnosis and treatment in young children. The commonest of these lesions seems to be congestion or hypertrophy of the verumontanum. Valves in their various forms are rare and most of them provide a grave clinical picture with gross bladder distension, back pressure and renal degeneration.

Institutional treatment for "functional" enuresis is of great value in selected cases, but any impressive reduction in the incidence can only come from preventive measures—better homes and better upbringing of children.

Mr. H. P. Winsbury-White: Chronic inflammatory changes in the posterior urethra and in the bladder are the commonest cause of disturbances of micturition at all ages and in both sexes. Routine cystoscopy and urethroscopy make this quite clear. Psychic and other influences from the central nervous system activate the involuntary act of micturition more effectively in the presence of cystitis and urethritis than when normal conditions exist.

The bladder is commonly involved by a spread of infection from the urethra. Often only the front of the trigone is affected (urethrotrigonitis).

In so-called functional enuresis the younger the child the more constantly are these signs of inflammation in the bladder present (70%, Winsbury-White, *Brit. J. Urol.*, 1941). In the older children and in many adults, the inflammation is commonly localized to the urethra (76%) or there is urethrotrigonitis, the more widespread inflammation having disappeared.

The cystitis is often only in patches (fig. 1). The changes in question are obviously inflammatory by comparison with the appearances seen in the terminal stage of frank cases of cystitis. The urine accompanying these changes commonly shows no evidence of infection.

Polypi, granulomata, dilated gland orifices are present in the urethra in many cases (figs. 2 and 3).

It is obvious from careful cystoscopy and urethroscopy in children with general disturbances of micturition that many cases of enuresis are simply part of a large group whose symptoms are due to inflammation involving the lower urinary tract, particularly the urethra (Spence and Moore, 1939; organic uropathy in 60% of 532 cases, Campbell, 1937). Important data bearing on urethral changes and enuresis are also forthcoming from a study of the three following groups in adults: (1) Those who suffered from enuresis
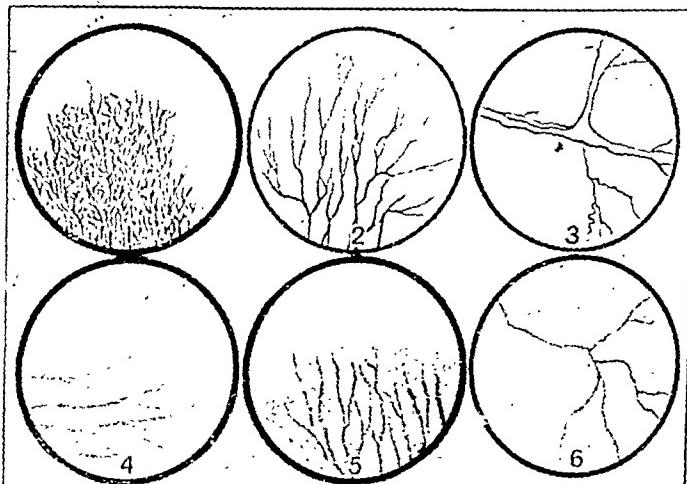
FIG. 1.—Photographs of coloured drawings made during cystoscopy of enuresis cases. 1. Vascular network marking posterior limit of trigone; note clear definition of individual vessels of uninflamed trigone (E. J., male, 14 years). 2. Vessels at back of uninflamed trigone (P. S., female, 11 years). 3. Vessels of uninflamed bladder wall; note clear definition of vessels (same case as No. 2). 4. Vessels at back of inflamed trigone; note the blurring of the outline of blood-vessels; no evidence of infection in urine (J. C., female, 6 years). 5. Similar to No. 4, i.e. blood-vessels in a patch of inflammation at back of trigone (J. W., female, 6 years; no evidence of infection in urine). 6. Blurred outlines of vessels of inflamed bladder wall; other patches of cystitis were also present; no evidence of infection in the urine; compare with No. 3.

FIGS. 2, 3 and 4 are photographs of coloured drawings made during urethroscopy. The views all depict chronic inflammatory changes.
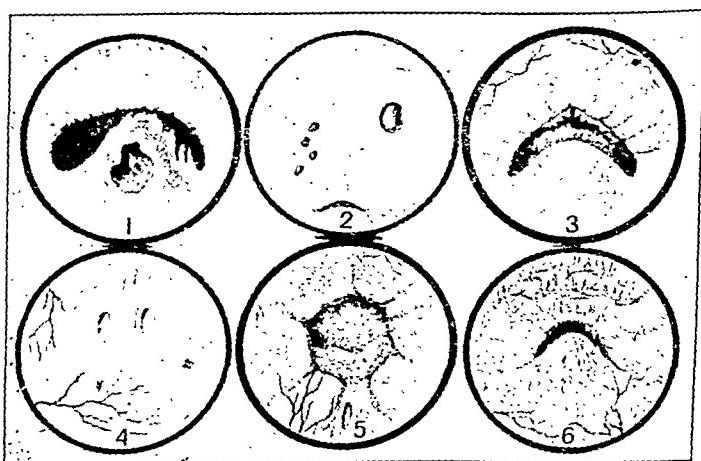

FIG. 2.—1. The changes involve the sinus pocularis, the verumontanum, and the left prostatic sinus (S. H., 8 years; meatitis at age of 2 years). 2. Gland orifices on roof of membranous urethra, dilated from past inflammation (same case as No. 1). 3. Filamentous inflammatory projections on roof of membranous urethra (K. M., 14 years; a male with enuresis). 4. Gland orifices dilated from chronic inflammation, on roof of membranous urethra (M. B., female, 2 years, 9 months; frequency, urgency and dysuria). 5. One of two adventitious gland orifices in posterior urethra is seen in the photograph (J. W., female, 6 years; with enuresis). 6. Tags of necrosed inflammatory tissue on roof of membranous urethra and on verumontanum (A. H., 44 years; enuresis for many years; 4 oz. residual urine).

in childhood only. (2) Those with whom enuresis has continued from childhood into adult life. (3) Those in whom enuresis commenced in adolescent or adult life (fig. 4).

Since the beginning of the war my own records show a great increase in the incidence of enuresis amongst male children. This coincides with the known increase of non-specific genital infections in the male sex during the same period. Inflammatory conditions of the genitals and variations in the calibre of the urethra in children which lead to enuresis have been dealt with by me in a previous publication (1941).

Contracted urethra.—This can be determined only from a knowledge of the size that the urethra should be, in relation to age (Winsbury-White, 1941). The condition is fairly common, and is generally the result of chronic inflammation.

Urethral inelasticity as indicated by variations in response to urethral dilatation is
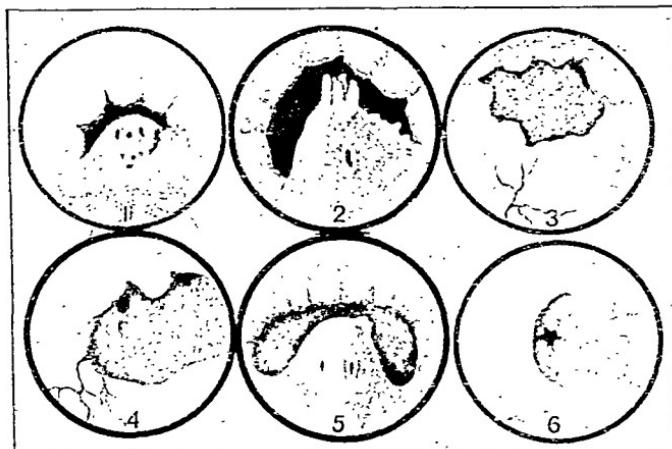

FIG. 3.—1. A granuloma in the left prostatic sinus ; several small pits present on the front of base of verumontanum (B. P., 11 years ; enuresis and attacks of frequency since early childhood).   2. Polypi on summit and granulomata on side of verumontanum (A. B., 12 years ; enuresis since early childhood).   3. Inflammatory hillocks on roof and right lateral wall of posterior urethra (see also No. 6) (G. H., male, 17 years ; enuresis and daily frequency since early childhood).   4. Inflammatory hillock on roof of posterior urethra (J. S., female, 13 years ; enuresis since early childhood).   5. Small granuloma on verumontanum (E. J., 14 years).   6. Stricture on right lateral wall of bulbous urethra ; and infected follicle (same as No. 3).
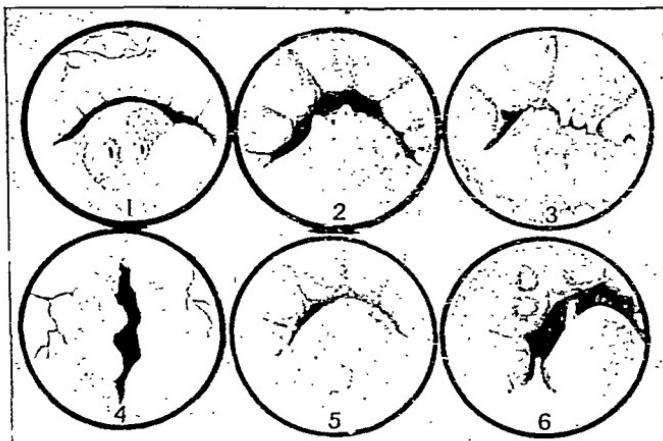

FIG. 4.—1. Large granuloma in left prostatic sinus (D. H., 22 years ; enuresis since age of 7 years ; residual urine : 2 oz.).   2. Collection of polypi on verumontanum (E. S., 18 years ; enuresis and frequency since early childhood).   3. Widespread inflammatory lesions in posterior urethra in region of verumontanum (A. C., 32 years ; enuresis since early childhood).   4. Inflammatory hillocks on right lateral wall of posterior urethra (F. S., 20 years ; male ; enuresis for 2 years).   5. Recent-looking inflammatory lesions on front of verumontanum (R. P., 22 years ; enuresis and frequency for 2 months ; residual urine : 3½ oz.).   6. Polypi on verumontanum and in right prostatic sinus and inflammatory patches on wall of posterior urethra (H. B., 35 years ; enuresis for 4 years).

also important, and the following extremes of dilatability of the urethra in the male were noted in enuresis cases:

Age of patient (in years)	...	...	...	5	9	13
Lowest dilatability (Charrière)	...	...	...	14	17	21
Highest dilatability (Charrière)	...	...	...	18	21	25

This is a group of cases which give a good response to treatment by urethral dilatation.

Intravenous urography commonly displays minor pathological changes in the upper urinary tract in enuresis cases (60%, Winsbury-White, 1941). Similar effects are noted in adults without enuresis who have chronic inflammation of the posterior urethra. These consequences frequently take the form of mild dilatations. Congenital dilatations are an obvious cause of enuresis in certain cases.

Residual urine is an important accompaniment of many cases of enuresis (16·2%, Campbell, 1937). Such cases are prone to attacks of urinary infection.

The urine.—There is plenty of evidence both experimental and clinical to substantiate the view that inflammation may be present in the urinary tract without corroboration of its presence in the urine (Thiele and Embleton, 1913; K. M. Walker, 1922; Cabot, 1936).

Treatment.—Selected cases respond favourably to urethral dilatation. A general anæsthetic should always be used for children.

Treatment by dilatation of a chronic focus of inflammation in the urethra, improves the condition by promoting drainage from the focus. In a series of cases previously published by me (1941), the results of treatment by this method were shown to be cessation of enuresis for periods varying from three months to two years in 58%.

Fulguration of urethral polypi is necessary in some cases. Successful treatment by urethral dilatation depends upon observing certain rules: (1) Special instruments for children should be used (Winsbury-White, 1941): (2) the cases should be selected by urethroscopy and cystoscopy; (3) meatotomy is first required in a large number of males; (4) a catarrhal condition in any system of the body contra-indicates treatment; it will cause a relapse when it occurs following treatment: (5) it is wise to delay treatment in very young patients; (6) a month should be the shortest interval between treatments: (7) several treatments may be necessary.

An extension of this paper, with further details of cases, will be published in the September number (1944) of the *British Journal of Urology*.

REFERENCES.

CAMPBELL, M. F. (1937) *Pediatric Urology*, 2, 373. New York.
SPENCE, H. M., and MOORE, H. (1939) *Texas St. J. Med.*, 35, 234.
WINSBURY-WHITE, H. P. (1941) *Brit. J. Urol.*, 13, 149.

Dr. Wilfrid Sheldon : Enuresis is by no means confined to the poorer sections of the community, but is met with throughout the social grades. While in young children it occurs about equally between the sexes, in the second half of childhood it is more common in boys than girls. In an inquiry among 5,000 children between 5 and 10 years of age, in well ordered, good Residential Homes for Poor Law Children, the incidence was found to be 5%. Three out of every five cases were boys.

I classify the cases into (1) Those associated with organic disease directly affecting the urinary tract. (2) Those in whom there is a disorder of health in some other system of the body, tending to promote or perpetuate enuresis. No child falling within either of these first two groups should be regarded as a functional enuretic.

The three remaining groups are: (3) Those in whom enuresis is associated with evidence of mental retardation. (4) Functional enuresis which has persisted from infancy. (5) Functional enuresis which has appeared in later childhood after an interval of some years in which the child has shown satisfactory sphincter control.

In the first group—besides children with deformities and infections of the urinary passages—are those in whom there is enuresis with pronounced polydipsia, such as is met with in diabetes mellitus, diabetes insipidus, and chronic interstitial nephritis. If nocturnal enuresis occurs, it is combined with either diurnal enuresis, or frequency of micturition, and this association is of clinical importance, because the functional nocturnal enuretic usually has good control of his bladder during the day.

If nocturnal enuresis is accompanied by diurnal frequency or actual enuresis, there is probably an underlying organic defect.

That persistent or recurrent infection of the urine is often associated with some underlying deformity of the urinary tract, is now common knowledge, and children showing such infection should be submitted to a complete urological investigation. I have yet to see the boy in whom enuresis could be attributed solely to phimosis. That spina bifida occulta is sometimes associated with intractable enuresis is probably true,

but operation on the spine for the cure of enuresis has little justification. Relief from enuresis is rarely obtained by reducing the acidity of the urine.

The treatment of enuresis should not be undertaken until a complete physical examination has been made.

The child whose enuresis is associated with chronic indigestion is not likely to learn dry habits until the digestion has improved. The output of urine in enuretic children is sometimes much greater during the night than by day, and I think this is sometimes to be attributed to persistent digestive upset. The perineal irritation caused by threadworm infection may possibly contribute to bed-wetting in much the same way as may balanitis, but more often the worm infection is part and parcel of an underlying chronic indigestion.

Children with allergic rhinitis often wet their beds, and that there is a close connexion between their allergic condition and their enuresis can often be demonstrated by the improvement in both conditions, either as a result of desensitization or by the employment of anti-allergic drugs as ephedrine. A tablet of ½ gr. given at bedtime over some weeks may banish enuresis. These children usually tolerate ephedrine very well, and if necessary the dose can be worked up to 1 or even 2 gr. at bedtime.

The young child whose wetting is associated with an ammoniacal smell to the bedding, and whose buttocks and perineum are reddened and sore requires a reduction of his fat intake, especially milk fat. This may be all that is required to enable the child to keep a dry bed.

Enuresis associated with mental retardation is most resistant to treatment. I refer not so much to the gross types of mental deficiency, with easily recognized physical stigmata, but to those children who are to be classed as dull and backward, unable to keep pace with their fellows, and with a poor capacity for concentration. It is often difficult to inculcate into these children a sense of right and wrong, and the methods of browbeating and intimidation are worse than useless. This calls for a strong but sympathetic personality in the parents, who often stand in need of our encouragement just as much as do the children. I think some form of bribery, such as a child will appreciate in return for a dry bed, may be legitimately used for these children. The use of drugs in this group is almost uniformly disappointing. Thyroid, which has been recommended in the treatment of enuresis, is in my experience as valueless in this group as in any other.

In those children, physically and mentally in good health, who have never learned to keep a dry bed, the original fault may lie in defective early training. Training should include the withholding of fluid after the tea meal, and forgoing the supper meal. The child should make a conscious effort to empty the bladder completely on retiring, and, if necessary, within an hour of going to bed. In any case they should be roused again after four hours to pass water, and this time of rousing should not vary from one night to the next. The rousing should be done thoroughly, so that the child knows what he is doing, and not be "sat out" while leaning against his mother, more asleep than awake. If the child wets in the early morning hours, a second rousing should be carried out after another four hours. This training may have to be carried out for a few weeks by the parents. Praise for a dry night is infinitely better than scoldings for a wet one.

Treatment by suggestion, such as belladonna in increasing doses, or a more powerful suggestion such as stretching the bladder by distension may help to bring about a cure.

Some children who have been dry for some years, may revert to persistent wetting at night. Often the trouble dates from some temporary lowering of health, such as an infectious fever; but the surprise and disappointment occasioned by the enuresis has so drained the child's self-confidence, that the wetting continues long after the initiating cause has been forgotten. These children are usually intelligent and sensitive, acutely conscious of their misfortune, and ready to be devastated by hard words or criticism. The fundamental object in dealing with these children lies in restoring their self-confidence either in hospital or in their own home; in the latter case, the parents' attitude must combine encouragement with unfailing confidence in their child's eventual recovery.

Lastly there is a small group that the war has brought to my notice, and that concerns evacuated children who intentionally wet their beds to gain some advantage such as being allowed to return home.

Dr. E. B. Strauss: Experiments have shown that even the smallest emotional experiences are accompanied by a contraction of the bladder. Urine and urinary activities, then, are possessed of powerful emotional and libidinal significance; and by far the greater number of cases of enuresis are of psychological rather than of urological import-

This is a group of cases which give a good response to treatment by urethral dilatation.

Intravenous urography commonly displays minor pathological changes in the upper urinary tract in enuresis cases (60%, Winsbury-White, 1941). Similar effects are noted in adults without enuresis who have chronic inflammation of the posterior urethra. These consequences frequently take the form of mild dilatations. Congenital dilatations are an obvious cause of enuresis in certain cases.

Residual urine is an important accompaniment of many cases of enuresis (16·2%, Campbell, 1937). Such cases are prone to attacks of urinary infection.

The urine.—There is plenty of evidence both experimental and clinical to substantiate the view that inflammation may be present in the urinary tract without corroboration of its presence in the urine (Thiele and Embleton, 1913; K. M. Walker, 1922: Cabot, 1936).

Treatment.—Selected cases respond favourably to urethral dilatation. A general anæsthetic should always be used for children.

Treatment by dilatation of a chronic focus of inflammation in the urethra, improves the condition by promoting drainage from the focus. In a series of cases previously published by me (1941), the results of treatment by this method were shown to be cessation of enuresis for periods varying from three months to two years in 58%.

Fulguration of urethral polypi is necessary in some cases. Successful treatment by urethral dilatation depends upon observing certain rules: (1) Special instruments for children should be used (Winsbury-White, 1941); (2) the cases should be selected by urethroscopy and cystoscopy; (3) meatotomy is first required in a large number of males; (4) a catarrhal condition in any system of the body contra-indicates treatment; it will cause a relapse when it occurs following treatment; (5) it is wise to delay treatment in very young patients; (6) a month should be the shortest interval between treatments; (7) several treatments may be necessary.

An extension of this paper, with further details of cases, will be published in the September number (1944) of the *British Journal of Urology*.

REFERENCES.

CAMPBELL, M. F. (1937) *Pediatric Urology*, 2, 373. New York.
SPENCE, H. M., and MOORE, H. (1939) *Texas St. J. Med.*, 35, 234.
WINSBURY-WHITE, H. P. (1941) *Brit. J. Urol.*, 13, 149.

Dr. Wilfrid Sheldon : Enuresis is by no means confined to the poorer sections of the community, but is met with throughout the social grades. While in young children it occurs about equally between the sexes, in the second half of childhood it is more common in boys than girls. In an inquiry among 5,000 children between 5 and 10 years of age, in well ordered, good Residential Homes for Poor Law Children, the incidence was found to be 5%. Three out of every five cases were boys.

I classify the cases into (1) Those associated with organic disease directly affecting the urinary tract. (2) Those in whom there is a disorder of health in some other system of the body, tending to promote or perpetuate enuresis. No child falling within either of these first two groups should be regarded as a functional enuretic.

The three remaining groups are: (3) Those in whom enuresis is associated with evidence of mental retardation. (4) Functional enuresis which has persisted from infancy. (5) Functional enuresis which has appeared in later childhood after an interval of some years in which the child has shown satisfactory sphincter control.

In the first group—besides children with deformities and infections of the urinary passages—are those in whom there is enuresis with pronounced polydipsia, such as is met with in diabetes mellitus, diabetes insipidus, and chronic interstitial nephritis. If nocturnal enuresis occurs, it is combined with either diurnal enuresis, or frequency of micturition, and this association is of clinical importance, because the functional nocturnal enuretic usually has good control of his bladder during the day.

If nocturnal enuresis is accompanied by diurnal frequency or actual enuresis, there is probably an underlying organic defect.

That persistent or recurrent infection of the urine is often associated with some underlying deformity of the urinary tract, is now common knowledge, and children showing such infection should be submitted to a complete urological investigation. I have yet to see the boy in whom enuresis could be attributed solely to phimosis. That spina bifida *occulta* is sometimes associated with intractable enuresis is probably true,

side of the thigh due to involvement of the obturator and sciatic nerves, and (c) by lymphatics which pass up between the rectum and peritoneum of the pouch of Douglas to the posterior abdominal wall; hence metastases in the bodies of vertebræ and certain tissues within the thorax.

There are three structures within the vicinity of the primary growth which are never invaded. These are the mucous membrane of the rectum, the vesiculæ seminales, and the triangular ligament. The illustration shows quite clearly how, in an extensive carcinoma,

Note triangular ligament as barrier to spread of cancer cells to perineum

Deposits in cancellous tissue of lumbar vertebræ.

Vertical section of prostate showing growth extending along cellular plane between the rectum and the pouch of Douglas ; the mucous membrane of the former has not been invaded. Note how cancer cells have surrounded the seminal vesicle but not penetrated its wall.

the cancer cells grip the seminal vesicle, but do not penetrate it, and travel along the submucous lymphatics of the rectum without causing ulceration of its mucous membrane. The triangular ligament is a powerful barrier, but its defence is weak at the point where it is in contact with the membranous urethra. Here are lymphatics just beneath the mucous membrane which occasionally convey cancer cells to the penis itself. On one occasion I mistook a growth in the glans penis for the primary lesion and was on the point of amputating the organ when it occurred to me to make a rectal examination. The whole picture was then revealed.

Accurate diagnosis often presents considerable difficulties. There are cases which on rectal palpation will leave no doubt in the mind of the clinician. They are the stony, hard mass, which, to the examining finger, seems to have no boundaries. A small fibro-adenoma can easily be mistaken for a malignant nodule, and vice versa. They can be enucleated with ease, and it may require a number of serial sections of the mass removed in order to demonstrate the presence of a carcinoma. Sometimes it is equally difficult to distinguish between chronic inflammation and cancer of the prostate. Both diseases spread beyond the capsule of the gland and give rise to impaired mobility on bimanual examination.

Cystoscopy and X-rays are valuable aids to accurate diagnosis, the latter demonstrates whether the hard nodules felt in the prostate are calculi and also whether there are any

ance. It is doubtful whether spina bifida occulta is found more frequently amongst enuretics than amongst others. The view that phimosis is of ætiological importance has little to support it, and circumcision as a method of treatment has nothing to commend it and must be regarded as psychologically dangerous. Drugs act by way of suggestion rather than through their pharmacological properties. It is possible to divide functional enuretics into primary and secondary groups. Primary enuretics give expression to primitive dispositions and drives by way of their symptom—infantile vesical pleasure, more highly libidinized pleasure, rage, aggressiveness, jealousy, a desire for love and protection, destructiveness and the like. They are interested and curious about the taps, tubes and holes of the body and what comes out of them. These preoccupations are so emotionally charged that they express themselves in sleep when the restrictive code of nursery morals and standards is lifted. The ideal form of treatment for the primary group is through uninhibited (and largely uninterpreted) play-activities in suitably equipped centres. About 50% of secondary enuretics respond well to hypnotic suggestion. In secondary enuresis the symptom is due to "secondary anxiety", by which is meant anxiety arising in connexion with emotionally over-determined anticipation of the symptom itself. "Secondary anxiety" is called secondary in this special instance because the primary anxieties which were supposedly the original cause of the symptom (enuresis, psychosexual impotence or whatever it may be) have faded into the background and have ceased to be of causal significance. The suggestions given are of two kinds: (1) Suggestions intended to allay secondary anxiety. (2) Suggestions designed to produce a kind of conditioned reflex in the bladder wall, which enables the bladder to act like its own alarm-clock, as it were, and wake the patient up in time to prevent accidents.

Since the war, enuresis has become a serious social problem, first amongst evacuated children who usually turn out to belong to the primary group of enuretics, and secondly amongst unwilling conscript soldiers who have learnt that they can successfully evade military service from the start by pleading enuresis. In this last group, it is very difficult to differentiate between the genuine case and the malingerer.

Wing-Commander J. C. Ainsworth-Davis : A great many cases of enuresis occur in the Service and I investigate them by cystoscopy, urethroscopy, and urine-analysis. In the vast majority of cases cystoscopy is normal except when the urine is infected. Very rarely is a median prostatic bar present. Urethroscopy I regard as a certain means of distinguishing between the congenital and the acquired cases. In the former, on withdrawing the urethroscope from the bladder, the roof of the internal meatus can be seen at the same time that the floor and the sides come into view, indicating a relaxed condition of the internal sphincter; whereas, in the latter, the roof can only be seen if the instrument is either depressed 45 degrees below the horizontal or if it is further withdrawn into the posterior urethra. As Mr. Winsbury-White has pointed out there is usually some abnormality to be seen in acquired cases, such as inflammatory projections of the internal meatus, polyposis of the verumontanum or evidence of chronic genital inflammation, which usually respond satisfactorily to dilatation, diathermy, or both.

No mention had been made of a possible operative cure of congenital enuresis by a gracilis transplant, or some other surgical procedure.

The President : The radiological finding of spina bifida occulta does not necessarily prove that this is the cause of enuresis. Cystoscopy, cystography, and cystometry will show any neurogenic lesion present, and in such cases exploration of the spine is some- . times indicated.

[*March 23, 1944*]

DISCUSSION : TREATMENT OF CARCINOMA OF PROSTATE

Mr. Clifford Morson : *The surgical treatment of carcinoma of the prostate.*—The pathology of carcinoma as it affects the prostate gland is peculiar in many respects. Its similarity to breast cancer is remarkable, in fact it is at times difficult to distinguish between the microscopic sections. Both form metastases in bone and both readily stimulate the formation of fibroblasts. The cancer cells from the prostate spread by three distinct paths: (a) By lymphatics which follow the course of the vas deferens to glands in the groin: hence the solid œdema of leg and lower abdomen met with on occasions. (b) By lymphatics in the pelvic cellular tissue which spread out fanwise from the base of the bladder towards the sciatic notch and iliac bone: hence the pain at the back and inner

side of the thigh due to involvement of the obturator and sciatic nerves, and (c) by lymphatics which pass up between the rectum and peritoneum of the pouch of Douglas to the posterior abdominal wall; hence metastases in the bodies of vertebræ and certain tissues within the thorax.

There are three structures within the vicinity of the primary growth which are never invaded. These are the mucous membrane of the rectum, the vesiculæ seminales, and the triangular ligament. The illustration shows quite clearly how, in an extensive carcinoma,

Note triangular ligament as barrier to spread of cancer cells to perineum

Deposits in cancellous tissue of lumbar vertebræ.

Vertical section of prostate showing growth extending along cellular plane between the rectum and the pouch of Douglas ; the mucous membrane of the former has not been invaded. Note how cancer cells have surrounded the seminal vesicle but not penetrated its wall.

the cancer cells grip the seminal vesicle, but do not penetrate it, and travel along the submucous lymphatics of the rectum without causing ulceration of its mucous membrane. The triangular ligament is a powerful barrier, but its defence is weak at the point where it is in contact with the membranous urethra. Here are lymphatics just beneath the mucous membrane which occasionally convey cancer cells to the penis itself. On one occasion I mistook a growth in the glans penis for the primary lesion and was on the point of amputating the organ when it occurred to me to make a rectal examination. The whole picture was then revealed.

Accurate diagnosis often presents considerable difficulties. There are cases which on rectal palpation will leave no doubt in the mind of the clinician. They are the stony, hard mass, which, to the examining finger, seems to have no boundaries. A small fibro-adenoma can easily be mistaken for a malignant nodule, and vice versa. They can be enucleated with ease, and it may require a number of serial sections of the mass removed in order to demonstrate the presence of a carcinoma. Sometimes it is equally difficult to distinguish between chronic inflammation and cancer of the prostate. Both diseases spread beyond the capsule of the gland and give rise to impaired mobility on bimanual examination.

Cystoscopy and X-rays are valuable aids to accurate diagnosis, the latter demonstrates whether the hard nodules felt in the prostate are calculi and also whether there are any

metastases in the bony pelvis. The X-rays do not often reveal the presence of deposits in the bodies of vertebræ.

Cystoscopy shows if there are nodules around the internal meatus and if there is œdema of the mucous membrane of the bladder base. In chronic inflammation these changes do not occur, nor are they observed in early malignant disease.

Biopsy, of course, is a certain way of establishing the diagnosis. A portion of the gland can be removed either by suprapubic cystotomy or transurethral resection. For such a purpose cystotomy is seldom justifiable. On account of the small amount of cancer tissue present in doubtful cases transurethral resection may also fail, but it is often worth the attempt. If, on catheterization there is a feeling of grittiness as the instrument passes along the prostatic urethra, this is a sure sign of malignant disease if the X-rays are negative to calculi. The measurement of residual urine does not help much, for the quantity retained in the bladder varies according to the type of growth, being absent in the scirrhous variety and present in the adenocarcinoma. It is variable in chronic prostatitis. Pain referred to the thigh and back, and the so-called "girdle" pain are sure indications of cancer. Progressive loss of weight is also another indication associated with it.

The surgical treatment may be divided into radical and palliative. The so-called radical operations are excision of the whole prostate and bladder base by either (a) the suprapubic route or (b) the perineal. The insertion of radium needles is another attempt to destroy the whole mass. Castration is the surgeon's method of practising hormone therapy: a very crude procedure. Then we have suprapubic cystotomy and transplantation of the ureters into the bowel, and transurethral resection which are performed for the relief of urinary obstruction, complete or incomplete. Finally there is enucleation of an adenomatous mass in which a malignant nodule is found on microscopic examination. The suprapubic and perineal excisions of cancer of the prostate are, in my opinion, unjustifiable operations. I speak from experience for I have performed them many times. Mr. Cyril Nitch in his paper on the conservative treatment of carcinoma of the prostate, which was read before the meeting of the International Society of Urology at Vienna in 1936, makes the following statement: "The brilliant results of Hugh Young in this field have not been attained by others, and Morson of London states in a recent paper that he has given up the radical operation he devised some years ago as the results were so disappointing. No patient survived longer than about five years; the expected duration of life of the untreated case." Nitch then goes on to say: "In an experience extending over twenty-five years I have come to the same conclusion, for I have seldom seen a case of undoubted carcinoma of the prostate in which I considered the risks of such a severe operation were justifiable."

The insertion of radium needles into the prostate by way of the perineum and bladder presents a different picture. The two techniques described by Nitch (Transactions of the International Society of Urology, VI Kongress, Wien, September 8-12, 1936) have given the following results:

Technique A, 20 cases.—One lived ten years and another lived eight years without signs of recurrence. One at the time of writing was alive and well, five years afterwards. The remaining 17 all died within three years, the average duration of life being one year ten months.

Technique B, 7 cases.—Two alive and well five years afterwards, with no signs of recurrence. Two alive and well three years after with no recurrence and two one and a half years after. One lived three years and then died with metastases in the bones.

My experience of radium treatment which dates from 1913 is similar to that of Nitch. No cases established as carcinoma survived five years. I have tried every known technique, the National Radium Commission having loaned radium to St. Peter's Hospital for this investigation.

I have nothing but condemnation for castration. All it does is to cause atrophy of the seminal vesicles and normal prostatic tissue. There is no scientific evidence that a single cancer cell is destroyed. Temporary improvement in micturition is brought about by the atrophy of normal tissue in the region of the prostatic urethra.

In an annotation with the title of "Castration for Cancer of the Prostate", in a recent issue of a medical journal, the writer stated that "it is common knowledge that bilateral castration leads to shrinkage of benign enlargements." He went on to say that on these grounds it was reasonable to hope that castration by causing atrophy of secreting cells and general deturgescence of the gland might relieve local tension and therefore mitigation of pain might be expected. After quoting Kretschmer's paper that there was no evidence of a permanent cure he went on to say: "We must have patience. Five or more years must be allowed to go by before a serious attempt can be made to assess the curative, as distinct from the palliative, value of this treatment". Here we have a number

of fundamental errors. In hyperplasia or adenomatous disease of the prostate bilateral castration causes no alteration in the size of the gland.

As for atrophy of secreting cells relieving pain the author is obviously unaware that carcinoma of the prostate is painless so long as the disease is confined within the gland capsule. Lastly by stating that five or more years must elapse before the curative value of this treatment can be assessed he has forgotten that William White of Philadelphia practised the operation in 1893. How much longer are we to wait before a definite opinion can be given?

The surgical treatment for obstruction consists of the choice of three procedures, suprapubic cystotomy, endothermy, either vesical or transurethral, and ureteric transplantation. The advantage of endothermy by the vesical route is that a large amount of growth can be excised by the cutting current. The disadvantage is that often the suprapubic wound will not completely heal, and there is intermittent leakage of urine. By the transurethral approach the obstruction can be temporarily relieved without any suprapubic interference. When retention recurs the operation can be performed again. The disadvantage is that endothermy, being an electric burn, promotes sepsis, and sepsis, super-imposed upon carcinoma, stimulates cancer cell proliferation. There may be also certain technical difficulties, owing to the size of the instrument. Ureteric transplantation into the bowel is a most satisfactory operation for the permanent relief of obstruction. Nitch has performed it with success and so have many others. Its only disadvantage is that a few patients have no resistance to the *Bacillus coli*, and we have no means of determining this before operation. The consequence is an early death from pyelonephritis. Finally there are the patients in whom a clinically malignant nodule has been overlooked in an adenomatous prostate and suprapubic enucleation has been carried out with success. Cases of this kind have been seen at St. Peter's Hospital, when ten or more years have elapsed before recurrence of the disease has been demonstrated. Experience of these cases brings us no nearer, however, to the solution of the problem of the cure of cancer of the prostate.

My considered opinion of the place of surgery in the treatment of this disease is that it should only be adopted for the relief of urinary obstruction. The choice lies between cystotomy, transurethral resection and ureteric transplantation into the bowel. The patient should be told the advantages and disadvantages of all three methods. My choice is a transurethral resection if it is technically easy, otherwise I favour cystotomy.

During the past twenty-five years I have made a special study of the course of this disease at a Municipal Hospital containing 1,200 beds. I have found that whatever treatment I have applied to the primary growth, very few cases survived longer than three years. The average number of admissions every year has been in the region of 50, but in nearly one-third of them the diagnosis has had to be revised. If the patient has been admitted with retention a cystotomy has been performed by the resident surgeon. These cases live in comparative comfort for about eighteen months, and then become bedridden and die within three years, riddled with metastases. In one case, in which I had performed the so-called radical operation, a recto-vesical fistula formed, and for three years the patient passed all urine and fæces through a suprapubic opening. An interesting fact was that in spite of the bladder having been a reservoir for all the excreta, the kidneys were found to be normal at the post-mortem. Another case survived five years after a radical operation, and during this time passed all his urine *per urethram*. He then died of a metastasis in the mastoid bone.

We should remember that accurate diagnosis is difficult in many cases without a biopsy; and secondly surgical interference with the primary growth, such as excision, resection, and the introduction of radium needles affords no hope of arresting the course of the disease.

Professor E. C. Dodds : Some years ago Huggins of Chicago showed that in a large series of cases of carcinoma of the prostate treated by castration, valuable results were obtained in a number of them, and in some the results were dramatic. He decided therefore to investigate very carefully the hormonal relationship of the prostate and of prostatic carcinoma.

It has been known for a long time that the growth of the prostate depends upon secretion from the testis and that the full development of the prostate can be regarded as a secondary sexual character. Thus in prepubertal castration, the prostate remains small and insignificant, and it may be developed by the injection of androgens. It has also been shown that œstrogens have a direct action on the prostate. If an animal be given doses of œstrogen over a prolonged period, enlargement of the prostate occurs and this may be counteracted by the administration of androgens. We have also the direct action of both these hormones upon the organ.

metastases in the bony pelvis. The X-rays do not often reveal the presence of deposits in the bodies of vertebræ.

Cystoscopy shows if there are nodules around the internal meatus and if there is œdema of the mucous membrane of the bladder base. In chronic inflammation these changes do not occur, nor are they observed in early malignant disease.

Biopsy, of course, is a certain way of establishing the diagnosis. A portion of the gland can be removed either by suprapubic cystotomy or transurethral resection. For such a purpose cystotomy is seldom justifiable. On account of the small amount of cancer tissue present in doubtful cases transurethral resection may also fail, but it is often worth the attempt. If, on catheterization there is a feeling of grittiness as the instrument passes along the prostatic urethra, this is a sure sign of malignant disease if the X-rays are negative to calculi. The measurement of residual urine does not help much, for the quantity retained in the bladder varies according to the type of growth, being absent in the scirrhous variety and present in the adenocarcinoma. It is variable in chronic prostatitis. Pain referred to the thigh and back, and the so-called "girdle" pain are sure indications of cancer. Progressive loss of weight is also another indication associated with it.

The surgical treatment may be divided into radical and palliative. The so-called radical operations are excision of the whole prostate and bladder base by either (*a*) the suprapubic route or (*b*) the perineal. The insertion of radium needles is another attempt to destroy the whole mass. Castration is the surgeon's method of practising hormone therapy: a very crude procedure. Then we have suprapubic cystotomy and transplantation of the ureters into the bowel, and transurethral resection which are performed for the relief of urinary obstruction, complete or incomplete. Finally there is enucleation of an adenomatous mass in which a malignant nodule is found on microscopic examination. The suprapubic and perineal excisions of cancer of the prostate are, in my opinion, unjustifiable operations. I speak from experience for I have performed them many times. Mr. Cyril Nitch in his paper on the conservative treatment of carcinoma of the prostate, which was read before the meeting of the International Society of Urology at Vienna in 1936, makes the following statement: "The brilliant results of Hugh Young in this field have not been attained by others, and Morson of London states in a recent paper that he has given up the radical operation he devised some years ago as the results were so disappointing. No patient survived longer than about five years; the expected duration of life of the untreated case." Nitch then goes on to say: "In an experience extending over twenty-five years I have come to the same conclusion, for I have seldom seen a case of undoubted carcinoma of the prostate in which I considered the risks of such a severe operation were justifiable."

The insertion of radium needles into the prostate by way of the perineum and bladder presents a different picture. The two techniques described by Nitch (Transactions of the International Society of Urology, VI Kongress, Wien, September 8-12, 1936) have given the following results:

Technique A, 20 cases.—One lived ten years and another lived eight years without signs of recurrence. One at the time of writing was alive and well, five years afterwards. The remaining 17 all died within three years, the average duration of life being one year ten months.

Technique B, 7 cases.—Two alive and well five years afterwards, with no signs of recurrence. Two alive and well three years after with no recurrence and two one and a half years after. One lived three years and then died with metastases in the bones.

My experience of radium treatment which dates from 1913 is similar to that of Nitch. No cases established as carcinoma survived five years. I have tried every known technique, the National Radium Commission having loaned radium to St. Peter's Hospital for this investigation.

I have nothing but condemnation for castration. All it does is to cause atrophy of the seminal vesicles and normal prostatic tissue. There is no scientific evidence that a single cancer cell is destroyed. Temporary improvement in micturition is brought about by the atrophy of normal tissue in the region of the prostatic urethra.

In an annotation with the title of "Castration for Cancer of the Prostate", in a recent issue of a medical journal, the writer stated that "it is common knowledge that bilateral castration leads to shrinkage of benign enlargements." He went on to say that on these grounds it was reasonable to hope that castration by causing atrophy of secreting cells and general deturgescence of the gland might relieve local tension and therefore mitigation of pain might be expected. After quoting Kretschmer's paper that there was no evidence of a permanent cure he went on to say: "We must have patience. Five or more years must be allowed to go by before a serious attempt can be made to assess the curative, as distinct from the palliative, value of this treatment". Here we have a number

HUGGINS, C. (1942) *Ann. Surg.*, 115, 1192.
——, and CLARK, P. J. (1940) *J. exp. Med.*, 72, 747.
——, and HODGES, C. V. (1941) *Cancer Res.*, 1, 293.
——, SCOTT, W. W., and HODGES, C. V. (1941) *J. Urol.*, 46, 997.
——, and STEVENS, R. E. (1940) *J. Urol.*, 43, 705.
——, ——, and HODGES, C. V. (1940) *New Orleans med. surg. J.*, 93, 121.
KUTSCHER, W., and WOLBERGS, H. (1935) *Z. f. physiol. Chem.*, 236, 237.
ROBISON, R. (1923) *Biochem. J.*, 17, 286.

Dr. W. M. Levitt: In the treatment of carcinoma of the prostate I shall describe what can be achieved by radiotherapy without other treatment. The assessment of the value of radiotherapy in the treatment of any deep cancer is not easy, since the variations in technique and outlook of individual radiotherapists are so great. Moreover, progress in radiotherapeutic technique has been so rapid that no single radiotherapist who has moved with the times can look back on a series of cases treated by a uniform method. Recent research by physicists in the field of radiation dosimetry has enabled us to achieve a very remarkable degree of accuracy in the direction of our beams of X-rays and in the localization of our X-ray dosage to any given region. The irradiation of a patient suffering from carcinoma has tended to become more and more a physical procedure carried out one fears, sometimes without due regard to the natural history of the spread of the disease and even without due application of clinical judgment to individual cases. In carcinoma of the prostate perhaps more than in any other kind of malignant disease, the indication is for irradiation of an adequate volume of tissue, even though the dosage may not be so high as is possible when the volume is limitied to the prostate and a very small shell of tissue surrounding it.

In a recent paper before the Faculty of Radiologists, I. G. Williams pointed out that in his series of cases of carcinoma of the prostate at the Middlesex Hospital the commonest sites for secondary deposits in bone were the vertebræ, especially the 4th and 5th lumbar, and the bones of the pelvic brim. He referred to the suggestion of Batson that the only anatomical system which fits the peculiar pattern of these bone metastases is the plexiform system of veins investing the sacrum, the lumbar spine and the wings of the iliac bones. Batson showed that the pelvic connexions of the deep dorsal vein of the penis are the same as those of the prostatic plexus. Thick radio-opaque material injected into the dorsal vein of the adult cadaver passed into the prostatic plexus, along the vessels of the lateral pelvic wall, and could be forced into the sacral canal and the veins of the iliac bones. The whole pattern is a replica of the spread of carcinoma of the prostate, and under certain conditions material injected in the dorsal vein could be made by direct spread to enter the veins in and about the sacrum and lumbar vertebræ and proceed up the spine eventually extending to the intercostal veins. If we can accept this account of the mechanism of metastatic formation in carcinoma of the prostate it is obvious that the indication in radiotherapy is for irradiation of a generous volume of tissue including the prostate and not for stricter and stricter limitation of the irradiation to the prostate itself. Thus, both highly concentrated small-volume irradiation by X-rays and irradiation by interstitial radium would seem, on theoretical grounds, to be inferior to radiation by X-ray therapy with larger fields. My own experience seems to bear out the theoretical considerations. I always irradiate practically the whole of the true pelvis, even in early cases.

40-50% of cases without known metastases improve considerably under radiotherapy. The symptoms improve until frequency and dysuria are completely, or almost completely, relieved. As a result of his better nights, the patient gains weight and feels fit. On examination, remarkable changes are found to have occurred in the prostate and in many cases so marked is the improvement that on rectal examination it would be impossible to say that the patient had ever had a carcinoma in the gland. Nevertheless, these gratifying results are not lasting. Their duration is variable. Some of the patients are carried off with metastases before they get local recurrences, but even if metastases do not occur, sooner or later nearly all the primary growths do recur. Sometimes these successful results only last for a few months; in other cases they may last for two, three or even more years. I have one or two cases which have been going long enough to permit the hope that there may be no recurrence. But these are the exceptions.

The X-ray treatment of carcinoma of the prostate is beset with many difficulties and calls for the exercise of considerable clinical judgment. The great bugbear is infection, and this is, of course, much more prone to occur with a suprapubic cystotomy, though it may occur without. Pain supervening in the course of treatment of carcinoma of the prostate is always of bad prognostic importance, especially so if the pain is of the trigone irritation type referred to the tip of the penis. Treatment should be interrupted immediately on the appearance of this symptom and very often relief can be obtained by chemotherapy at this stage. In weak and elderly patients especially there is a danger of ascend-

The composition of prostatic secretion has been shown to contain a number of substances of an unexpected or unusual character. The most important from our present point of view is the phosphatase which acts best on the acid side of neutrality. The phosphatases—i.e. enzymes capable of splitting up organic compounds of phosphorus such as glycero-phosphates and the phosphate carbohydrate compounds—have been known for many years. They were first described in 1912 by Grosser and Husler in the kidney. In 1923, an extensive series of investigations were undertaken by Robison who showed that these ferments played a very important part in the calcification of bone. The optimum hydrogen ion in their activity was usually well on the alkaline side of neutrality. It was not until 1934 that Davies, Bamann and Riedel showed that there was a second phosphatase present in some tissues whose maximum activity was shown at a pH of 4·8. In 1935 Kutscher and Wolbergs showed that prostatic tissue was very rich in this acid phosphatase. In 1936 the Gutmans *et al.* commenced a long series of investigations which showed that the phosphatase content of the prostate was in a way a measure of its activity and that some of the phosphatase escaped into the serum. In castration of normal animals or man the acid serum phosphatase is low and can be raised by the injection of androgens. In carcinoma of the prostate, very high figures were obtained, and if such cases were castrated the acid serum phosphatase fell with a concomitant improvement of the symptoms. It would appear therefore that the acid serum phosphatase is a method of diagnosing carcinoma of the prostate and of assessing the progress of treatment. There is a little difference of opinion on the normal acid serum phosphatase content. The most recent views of Huggins *et al.* are that anything below 3·25 units per 100 c.c. should be regarded as normal. In this country we usually consider 2·5 units to be the upper limit. It may well be that there are certain differences in technique that explain this slight divergence. Between 5 and 10 units give a strong suspicion of carcinoma of the prostate, whilst over 10 is diagnostic. Experience has shown that higher figures are obtained in patients with metastases.

The objections to castration are so obvious that one need not spend time discussing them. The possibility of producing an inhibition of the testis secretion by physiological means was considered. It has been known for some considerable time that large doses of œstrogens would inhibit the anterior lobe of the pituitary and prevent the production of gonadotrophic hormone. Huggins, therefore, treated some cases by injection of œstradiol benzoate subcutaneously. Excellent results were obtained, but it is of course essential to maintain the subcutaneous injections over a prolonged period. It was natural that he should try to obtain the same results with the orally active synthetic œstrogen stilbœstrol. This substance, first produced in 1938 by my colleagues and myself, has been shown to possess all the biological activities of the naturally occurring œstrogens, and at the same time to be highly active by mouth. It is moreover very cheap and can therefore be used on any scale more or less regardless of price. There now exists in the American literature descriptions of a series of cases of carcinoma of the prostate treated with stilbœstrol in which not only have the local symptoms completely disappeared, but the secondary deposits have also come under control. A bedridden invalid with severe nerve symptoms due to pressure of secondary deposits, was rendered completely normal and returned to his work.

Dosage.—One can proceed in two ways: empirically, commencing with 1 mg. three times a day and increasing to 5 or more until the symptoms come under control. Alternatively, one can watch the progress of the treatment by the estimation of the acid serum phosphatase. Once this has been reduced to normal limits, we have been surprised at the small amount of stilbœstrol required to maintain the patient symptom-free. As to which synthetic œstrogen is to be recommended, I am afraid that at present we have not sufficient experience. The impression is current amongst most clinicians that dienœstrol is the most active and the least likely to give side effects such as nausea, and that hexœstrol occupies a position midway between dienœstrol and stilbœstrol.

Finally, it cannot be too strongly emphasized that no single member of the workers in this field has ever claimed that this treatment represents a cure. It would appear that a very large number of cases can be rendered symptom-free by the administration of synthetic œstrogens; as to how long this can continue it is not possible to say although cases have been maintained in perfect health for periods of over three years. Regarding mechanism it is as yet too early to make any statement, but there can be little doubt that the whole series of observations open up an entirely new and interesting approach to this problem.

REFERENCES

BAMANN, E., and RIEDEL, E. (1934) *Z. f. physiol. Chem.*, 229, 125.
DAVIES, D. R. (1934) *Biochem. J.*, 28, 529.
GROSSER, P., and HUSLER, J. (1912) *Biochem. Z.*, 39, 1.
GUTMAN, E. B., SPROUL, E. E., and GUTMAN, A. B. (1936) *Amer. J. Cancer*, 28, 485.

HUGGINS, C. (1942) *Ann. Surg.*, **115**, 1192.
——, and CLARK, P. J. (1940) *J. exp. Med.*, **72**, 747.
——, and HODGES, C. V. (1941) *Cancer Res.*, **1**, 293.
——, SCOTT, W. W., and HODGES, C. V. (1941) *J. Urol.*, **46**, 997.
——, and STEVENS, R. E. (1940) *J. Urol.*, **43**, 705.
——, ——, and HODGES, C. V. (1940) *New Orleans med. surg. J.*, **93**, 121.
KUTSCHER, W., and WOLBERGS, H. (1935) *Z. f. physiol. Chem.*, **236**, 237.
ROBISON, R. (1923) *Biochem. J.*, **17**, 286.

Dr. W. M. Levitt : In the treatment of carcinoma of the prostate I shall describe what can be achieved by radiotherapy without other treatment. The assessment of the value of radiotherapy in the treatment of any deep cancer is not easy, since the variations in technique and outlook of individual radiotherapists are so great. Moreover, progress in radiotherapeutic technique has been so rapid that no single radiotherapist who has moved with the times can look back on a series of cases treated by a uniform method. Recent research by physicists in the field of radiation dosimetry has enabled us to achieve a very remarkable degree of accuracy in the direction of our beams of X-rays and in the localization of our X-ray dosage to any given region. The irradiation of a patient suffering from carcinoma has tended to become more and more a physical procedure carried out one fears, sometimes without due regard to the natural history of the spread of the disease and even without due application of clinical judgment to individual cases. In carcinoma of the prostate perhaps more than in any other kind of malignant disease, the indication is for irradiation of an adequate volume of tissue, even though the dosage may not be so high as is possible when the volume is limitied to the prostate and a very small shell of tissue surrounding it.

In a recent paper before the Faculty of Radiologists, I. G. Williams pointed out that in his series of cases of carcinoma of the prostate at the Middlesex Hospital the commonest sites for secondary deposits in bone were the vertebræ, especially the 4th and 5th lumbar, and the bones of the pelvic brim. He referred to the suggestion of Batson that the only anatomical system which fits the peculiar pattern of these bone metastases is the plexiform system of veins investing the sacrum, the lumbar spine and the wings of the iliac bones. Batson showed that the pelvic connexions of the deep dorsal vein of the penis are the same as those of the prostatic plexus. Thick radio-opaque material injected into the dorsal vein of the adult cadaver passed into the prostatic plexus, along the vessels of the lateral pelvic wall, and could be forced into the sacral canal and the veins of the iliac bones. The whole pattern is a replica of the spread of carcinoma of the prostate, and under certain conditions material injected in the dorsal vein could be made by direct spread to enter the veins in and about the sacrum and lumbar vertebræ and proceed up the spine eventually extending to the intercostal veins. If we can accept this account of the mechanism of metastatic formation in carcinoma of the prostate it is obvious that the indication in radiotherapy is for irradiation of a generous volume of tissue including the prostate and not for stricter and stricter limitation of the irradiation to the prostate itself. Thus, both highly concentrated small-volume irradiation by X-rays and irradiation by interstitial radium would seem, on theoretical grounds, to be inferior to radiation by X-ray therapy with larger fields. My own experience seems to bear out the theoretical considerations. I always irradiate practically the whole of the true pelvis, even in early cases.

40-50% of cases without known metastases improve considerably under radiotherapy. The symptoms improve until frequency and dysuria are completely, or almost completely, relieved. As a result of his better nights, the patient gains weight and feels fit. On examination, remarkable changes are found to have occurred in the prostate and in many cases so marked is the improvement that on rectal examination it would be impossible to say that the patient had ever had a carcinoma in the gland. Nevertheless, these gratifying results are not lasting. Their duration is variable. Some of the patients are carried off with metastases before they get local recurrences, but even if metastases do not occur, sooner or later nearly all the primary growths do recur. Sometimes these successful results only last for a few months; in other cases they may last for two, three or even more years. I have one or two cases which have been going long enough to permit the hope that there may be no recurrence. But these are the exceptions.

The X-ray treatment of carcinoma of the prostate is beset with many difficulties and calls for the exercise of considerable clinical judgment. The great bugbear is infection, and this is, of course, much more prone to occur with a suprapubic cystotomy, though it may occur without. Pain supervening in the course of treatment of carcinoma of the prostate is always of bad prognostic importance, especially so if the pain is of the trigone irritation type referred to the tip of the penis. Treatment should be interrupted immediately on the appearance of this symptom and very often relief can be obtained by chemotherapy at this stage. In weak and elderly patients especially there is a danger of ascend-

ing infection if treatment is not interrupted immediately on the appearance of this symptom. Moreover in such patients X-ray dosage should be low and only very cautiously increased as the treatment proceeds. The whole position in the treatment of infected cases of carcinoma of the prostate has been altered by the advent of the sulphonamides. Prontosil is the best preparation because it is excreted in highest concentration in the urine and small doses only are necessary in most cases. I use ½ g. twice daily on the earliest signs of vesical irritation and these doses do not cause depression or nausea.

The function of radiation in the treatment of secondary deposits in carcinoma of the prostate is frankly palliative. So long as the deposits remain few and isolated pain can be more or less completely relieved and recalcification induced. This is now a matter of common experience and needs no elaboration. Unfortunately once secondary deposits in bone have appeared they very soon become multiple and too widespread for any hope of adequate irradiation. It is sometimes worth while irradiating selected deposits, such as deposits in the spine, in the hope of avoiding paraplegia. It is, however, probable that in general in the treatment of metastases of carcinoma of the prostate X-ray therapy will be superseded by hormone therapy.

In a fair proportion of cases of carcinoma of the prostate the growth can, by irradiation, be so severely damaged without undue damage to the healthy tissues and without undue risk to the patient as to lead to its apparent total regression and to paralyse its growth for a variable period. Apparently a similar result may be brought about by the use of œstrogens, the effect of which is undoubtedly to damage the carcinoma cells. It has been suggested that X-rays may act, at least in part, by causing castration, but, in fact, good results have often been obtained in cases in which the testes have been carefully protected. Moreover, the interstitial cells are not affected by radiation. It is reasonable to suppose that the mode of production of the damage by the two types of treatment is not the same, therefore by combining the two forms of treatment a summation of damage to the carcinoma cells may be produced which may give us in a proportion of cases a lasting result. Certainly there seem to be sufficient grounds for a thorough trial of the method.

My experience in three cases treated by the combined method of œstrogen therapy and irradiation is that patients do not tolerate X-ray therapy quite so well if it is being applied at the same time as œstrogen therapy. In combining the two methods the treatment should begin with one of the œstrin preparations working up to fairly high dosage, say 200 to 250 mg. over three weeks. Œstrin therapy should then be interrupted and X-ray therapy commenced. The X-ray dosage should be rather smaller than normal to begin with and worked up cautiously to the average rate. An attempt should be made to get in full X-ray dosage. Thereafter the acid phosphatase may be used as a guide to the administration of further chemotherapy.

Lieut.-Colonel W. L. Harnett, Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign, brought forward statistics collected by the Committee from all the London Hospitals, of the results of treatment of carcinoma of the prostate. Of 15,200 cases of cancer registered during the 17 months from April 1, 1938, to September 3, 1939, when the registration of new cases ceased, there were 382 cases of primary carcinoma of the prostate. The mean age of the patients was 67·4 years and 139 of them were over 70 years of age, a fact which must be taken into consideration in assessing the results of treatment.

For tabulation, the cases were divided into three clinical stages, I, those in which the growth appeared to be still within the capsule of the prostate, which was freely movable; II, those in which the growth had extended beyond the capsule and the gland was more or less fixed; III, those in which there was clinical evidence of distant metastases.

The *types of treatment* employed in the three stages are shown in Table I.

TABLE I.

	Stage I	Stage II	Stage III	Total	Operation mortality
Number of cases	80	190	112	382	
Radical surgical	30	8	—	38	2 (5·2%)
Palliative surgical	34	110	15	159	29 (18·2%)
Radiotherapy (including 3 by implantation of radium)	6	32	23	61	13 (21·3%)
Not treated	10	40	74	124	

Prostatectomy by any method is included in the "radical surgical" group, which also includes 35 cases which were diagnosed as benign prostatic enlargements and were discovered to be malignant when microscopically examined. "Palliative surgical" comprises

suprapubic cystotomy, endoscopic resection and radical operations which were abandoned. Any patient who died within one month of operation is counted as an operation fatality. All patients who died shortly after the completion of a course of radiotherapy were counted as the operation mortality of that form of treatment. There were 40 cases in which the appearance of a secondary growth was the first sign and led to the discovery of a symptomless primary.

The *results of treatment,* as far as at present known, on the basis of a four-year follow-up for the 1938 cases and three-year for the 1939 cases are shown in Table II.

TABLE II.

				Radical surgical	Palliative surgical	Radio-therapy	Not treated	Totals
Died in 1st year	...	...	...	8	91	33	93	225
,, 2nd ,,	...	...	...	9	28	12	15	64
,, 3rd ,,	...	...	...	2	8	6	3	19
,, 4th ,,	...	...	...	4	3	3	—	10
Alive at end of 3rd year	...	...	6	4	3	1	14
,, ,, 4th ,,	...	...	2	14	1	1	18
Untraced	...	...	...	7	11	3	11	32
				38	159	61	124	382

To assess the results of treatment on a sound statistical basis, it is necessary to allow for the varying expectation of life in groups of patients of different ages. The method of using a life table to calculate the mean normal expectation of life over a three, four or five-year period of observation of a group of persons of the same ages as the group under consideration, and then the working out of the ratio of the mean *actually* lived to the mean *expected,* was explained. Calculated in this manner it was found that the mean duration of life in the group treated by prostatectomy was thirty-one months, which was 77% of expected; in those treated by palliative methods or by radiotherapy it was twenty-three months or 55% of expected, whilst those not treated lived fourteen months or 33% of expected. These figures were only preliminary, however, and would probably not appear so good when the full five-year follow-up was available.

In conclusion, the speaker thanked the Chairman of the Clinical Cancer Research Committee of the British Empire Cancer Campaign for permission to bring forward figures as yet unpublished.

Mr. **Kenneth Walker** stated that there was only one point on which he disagreed with Mr. Clifford Morson, namely, on the subject of castration. He had found subcapsular removal of the testicles of great benefit in certain cases of carcinoma of the prostate. It provided a good alternative in cases in which there was difficulty in giving stilbœstrol. The fact that castration had been abandoned as a method of treating prostatic obstruction when it had been used during the last century was of no importance. Nor were theoretical arguments against it of any account. Medicine and surgery were still empirical arts, and we employed many remedies without knowing how they acted.

Mr. **Terence Millin** based his experiences of hormone therapy on some 92 cases treated by subcapsular orchidectomy, stilbœstrol, or both. The immediate results were dramatic in fully 90% of cases; those which before the advent of the therapy would have required transurethral resection, cystotomy, or even colostomy, escaped surgical intervention owing to the rapid resolution of the enlarged gland. He now reserved transurethral resection to those cases where a cystotomy had been established, and in which a restitution of normal micturition seemed possible. This was rapidly achieved by a combination of resection and subcapsular orchidectomy. In his experience only a small proportion of bony metastases had disappeared. He detailed one remarkable case, and showed films of a pelvis formerly riddled with secondaries now radiologically free. The dose of stilbœstrol employed was usually 5 mg. daily for two to three weeks, followed by 2 to 3 mg. daily indefinitely. The chief complaint from the use of the hormone was mastodynia with œdema of ankles, nausea, hot flushes, and lack of libido. The treatment constituted a great advance, but was not apparently curative, as deaths were now occurring in those treated more than two years.

Mr. **E. W. Riches** said he had treated 24 patients during the past year with favourable results, giving up to 15 to 20 mg. of stilbœstrol daily. Control by phosphatase estimations and histological verification by endoscopic resection were important in the present stage of our knowledge. About 50% developed mastitis after 500 to 600 mg., but it was not severe. He showed X-rays indicating regression of pulmonary metastases after treatment.

Mr. G. E. Vilvandré cautioning against enthusiasm, mentioned a man with secondaries of the prostate in the sacrum and spine who was given little X-ray treatment and who was alive and working (secondaries and all) some years later.

Mr. Alex. E. Roche said that he would not recommend removal of the testicles without disclosing the diagnosis of carcinoma which he was loth to do.

Mr. Hugh Donovan said he had treated 14 patients with encouraging results. After hearing Dr. Levitt he proposed to supplement stilbœstrol treatment with deep X-rays in alternate patients. 5 mg. of stilbœstrol t.d.s. often relieved retention, but it took time—perhaps three weeks. In three cases he noted symptoms of cardiac failure—possibly a coincidence.

Mr. Kenneth Heritage said that symptomatic relief following the use of stilbœstrol was often most dramatic, but when this failed or was tardy in appearance he did not hesitate to do a bilateral subcapsular orchidectomy. This operation caused only minimal cosmetic change, and so far had never failed to relieve symptoms. Its finality was also an advantage. Recrudescence of the growth could not be due to orchitic hormone. Diagnosis in the less advanced cases was a problem. Transurethral biopsy might not reach the carcinoma in the posterior lobe. Needle biopsy by Silvermann's needle might be more suitable.

Dr. L. R. Woodhouse Price stated that he had made a diagnosis of malignant prostate in many cases by means of immediate frozen sections of material removed by endoscopy. It was preferable that several pieces of biopsy tissue should be available, but it was equally true that several sections should be examined in cases of suprapubic prostatectomy. With reference to aspiration material, he had successfully established a diagnosis in several cases using wet-film fixation.

Mr. J. Gabe said that earlier diagnosis was essential. He had recently seen a man with multiple bone metastases who had not previously had a rectal examination. This examination was necessary in all men over 50 who had persistent pain in the thigh or back. He had found stilbœstrol of value in about half of his cases. The dose he gave was 5 mg. t.d.s.

Mr. Morson, in answer to criticisms of his condemnation of castration, pointed out that the operation, having been resurrected at intervals during the past fifty years, was no solution of the problem of a cure for prostatic carcinoma. Breast cancer had been also treated by removal of both ovaries with equally unsatisfactory results. The excision of portions of the testicle was merely a concession to the patient who objected to being sexually maimed. The effect of synthetic œstrogen therapy was in a totally different category. Whereas castration only had an action on normal sexual tissue, such a drug as stilbœstrol often had immediate dramatic results referable not only to the primary growth but also to metastases. He described a number of cases which had become symptom-free within a week of the commencement of the treatment together with absorption of the major part of the primary growth. Unfortunately the improvement was not always maintained. His advice was that in all cases, both of clinically definite carcinoma and those where the diagnosis was uncertain, immediate treatment with stilbœstrol (3 mg. every four hours) should be given, and continued until the patient is symptom-free, when the dose can be reduced.

Section of Ophthalmology

President—F. A. JULER, F.R.C.S.

[*February* 11, 1944]

Embolism of Right Inferior Retinal Arterial Division.—HUMPHREY NEAME, F.R.C.S.

S. G., aged 23. Housewife.

History.—17.3.42: Seen at Moorfield's Eye Hospital with a history of migraine. Corrected vision 6/9 both eyes. After homatropine and cocaine retinoscopy, post-mydriatic test R. with −2·25 sph., −0·25 cyl., 180° = 6/9, 6/6 (partly); L. with −2·75 sph., −0·25 cyl., 180° = 6/9, 6/6 (partly).

29.12.43: The patient complained of partial loss of sight in the right eye for five days. It was ushered in with a migraine phenomenon with coloured lights. She gave a history of occasional complete "blackout of one eye" lasting for a second, and then the appearance of spots lasting for about ten minutes, followed by severe headache. The history is suggestive of migraine.

Examination of the right fundus showed a cloudy area of retina occupying the inferior temporal quadrant and part of the inferior nasal. Retinal vessels near the disc
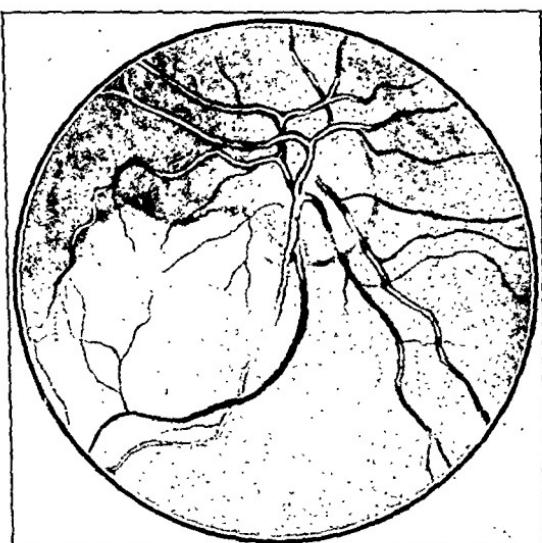
Embolism of right inferior retinal arterial division.

somewhat obscured. With right pupil dilated R.V. with lens is 6/60 with eccentric fixation. L.V. with lens 6/6. A pale yellowish-coloured block is seen in the inferior temporal artery at its division from the inferior nasal (*see* figure).

Examination by physician revealed nothing abnormal in the circulatory system. B.P. 130/80. Bleeding time 3¾ minutes. Coagulation time 1 minute 50 seconds. W.R. negative.

2.2.44: The yellowish block is much less clear, but a bright reflection is seen on the somewhat enlarged artery at that site. The artery wall is visible as a pale greyish border on the optic disc. The colour of the fundus below is now normal. Bjerrum screen

shows loss of upper half field to 2/2,000 white. R.V. with lens 6/18 by fixing the 6/36 line, not with direct fixation.

Mr. Neame said that when he first saw this patient the fundus was very white, but that had now almost disappeared, the fundus was now just a little mottled in the lower part. As it was five days after the onset of the visual loss when he saw her it seemed useless to apply any treatment such as paracentesis and massage of the eye.

In reply to the President, who referred to a recent case reported in the *Journal of Ophthalmology* and asked whether Mr. Neame had had any experience of injections in the early stages after a blockage, Mr. Neame said that a good many years ago he had a man aged 60 who came up within twenty-four hours of an affection of his sight from central arterial obstruction. (The same trouble had occurred in the other eye six months before.) He gave him amyl nitrite, with no effect, and then paracentesis and massage, and his vision improved to 6/18 from hand movements or counting fingers. Therefore it seemed that the embolus within twenty-four hours was moved on by this procedure. When this man first came up he still showed in the other eye the signs of central arterial obstruction.

Mr. R. Lindsay-Rea said that after reading of the effects produced by the administration of mecholyl on the cardiovascular system he thought it exceedingly dangerous to employ the drug, especially as the results on the eye were so meagre. Several times he had injected acetylcholine subconjunctivally, but the brawny œdema of the conjunctiva together with the pain of which the patients complained for weeks and the poor results made him hesitate to try this method again. Perhaps he might inject the acetylcholine far back into the orbit to get a more direct effect on the artery without hurting the eyeball.

The patient shown by Mr. Neame had mentioned she had suffered from rheumatic fever which had left a valvular murmur; hence the origin of the embolism which occupied the lower branch of the artery. It was indeed fortunate that it was not the upper branch. She had told him it had occurred shortly after childbirth.

Mr. Neame said that she was examined by the physician at Moorfields, who reported her chest and abdomen clear.

Mr. W. H. McMullen said that a man in the early sixties came to him with a history of sudden failure in the right eye a few hours previously. He had slight perception of light only in the extreme periphery of the temporal field, and there was a typical picture of blockage of the central artery. The failure had taken place at eleven in the morning, and some degree of white opacity with dark spot at the macula was already present at three in the afternoon when he made the examination. He gave a subconjunctival injection of 0.1 g. of acetylcholine, and within forty minutes there was considerable recovery of vision but with much restriction of nasal field; on the following day there was almost a full field of vision. After ten days the peripheral limits of the field for a ¼° test object were normal, but central vision had not recovered. Visual acuity was 3/60.

Bilateral Ptosis and Atypical Slant Eyes Associated with Unilateral Syndactyly, Adactyly and Brachyphalangy. A Note on the Genetics of the Case.—D. V. GIRI.

On 23.1.44, D. B. D., male, aged 18, consulted Mr. Giri because of headaches. Low oblique astigmatism corrected. Nothing unusual in the globes. Lids: Palpebral apertures narrow, right greater than left, and obliquely set with the internal canthi lying higher than the external.

The left hand: The thumb and index fingers are syndactylous throughout; because of this the thumb is bent at the phalangeal joint and the index finger, which seems to have only two phalangeal bones, the distal one of which is poorly developed, is curved towards the thumb and prevented from attaining greater length than the thumb:

Ptosis. Atypical slant eyes.

Developmentally defective hand.

there are two nails which are fused into a ridge where they meet and are somewhat concave laterally on either side of the ridge. The middle and ring fingers are absent and the little finger, which has only two phalanges, appears stouter than normal. There is plenty of power, flexibility and manipulative skill in the hand. It appears there is no other abnormality in the body.

The father has atypical slant eyes similar to the patient's, but no ptosis and the mother has bilateral ptosis, but the eyes show no slant. The patient has two brothers one elder and one younger. The younger has no abnormality; the elder, except for being unusually tall—6 ft. 6 in.—has no genetic abnormality. No evidence of heredity in the parental pedigrees.

It is probable that some or all of the abnormalities, either modified or unmodified, will be inherited by some of the patient's progeny, and by all, if the mate also contributes similar abnormal genes.

Mr. O. Gayer Morgan said that from a eugenic point of view this condition was not a very serious one as it only produced a very slight facial disfigurement and a defective hand on one side. There was no mental deficiency. Thus there was probably no need to advise against marriage in this case.

Left Corneal Foreign Body (Glass Splinter) Projecting into Anterior Chamber.—VICTOR PURVIS, M.B.

L. S., male, aged 14.

History (16.2.39).—The patient broke his spectacles and a small piece of glass became embedded in the left cornea.

On examination.—Left eye: Glass found to be embedded in deeper layers of cornea and projecting for the greater part of its length into the anterior chamber. Lens and vitreous clear. Fundus normal. Vision, with correction = 6/9.

It was decided at the time to make no attempt to remove the glass, and the eye has remained unchanged ever since.
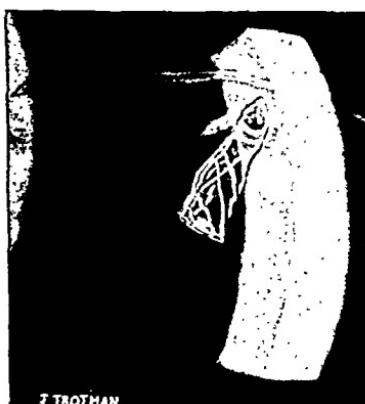
L.S., aged 15. 8.2.44.

The glass can now be seen projecting into the anterior chamber in exactly the same position as in 1939, and demonstrates the possibility of glass remaining in an eye without causing any attacks of inflammation (*see* figure).

Two Cases of Central Venous Thrombosis.—VICTOR PURVIS, M.B.

These cases demonstrate the difficulty of making a diagnosis of this condition when it is of long standing. In the one case there was massive exudation, the hæmorrhages having mostly absorbed; and in the other case hæmorrhages and exudates had completely absorbed leaving two areas of retinal cystic formation, at the macula and over the nasal half of the disc. This cystic degeneration of the retina in the second case is not common, but is of great interest, for it has all the appearances of a localised detachment.

The Micro-Diagnosis of Conjunctivitis Artefacta

By JOHN FOSTER, F.R.C.S.

CONJUNCTIVITIS artefacta is a term of uncertain meaning [18]. I would define it as conjunctivitis knowingly self-produced to obtain sympathy, compensation, or evasion of military service. Historically the first type is as old as hysteria and mendicancy, the second as the Workmen's Compensation Act, and the third was the subject of a mass prosecution in the French Army of 1807. .

Diagnosis by microscopic identification of the causative agent was foreshadowed by Conan Doyle's "Monograph on 114 varieties of cigar ash" mentioned in the "Sign of Four", but was first applied systematically to conjunctivitis by the French in the last war. The method has the advantage of rapidity, and with a little organization, of simplicity. I found in practice the chief difficulties of application are due to (1) Difficulties in collecting and preserving specimens. (2) Lack of proper though simple apparatus and reagents at the material time. (3) Vague or absent description of the microscopy of some irritants. To appreciate the use and limitations of the method conjunctivitis artefacta must be shortly considered.

Method of Production [9].—The irritants recorded in the literature are most varied, ranging from leech bites [7] to insertion of dental tartar and transfer of trachoma. Traditional knowledge (an individual may produce a local epidemic) based on a desire to avoid permanent injury to sight, and accessibility of material such as condiments. limits the cause as a rule in Allied Territory to the list given below, in which signs peculiar to specific irritants are mentioned. This enables a study of the microscopy of most possible agents to be made in advance.

The general characteristics, though not invariable, are as follows: (1) Improbable ætiology, and unexpected relapse. (2) Exacerbation by ordinary treatment. (3) Secretion catarrhal rather than purulent. (4) Purulent discharge if present most marked in the morning [4]. (5) Striking chemosis with subconjunctival hæmorrhage and little discharge [10]. (6) Unilateral. (7) Predominantly affecting lower lid and lower half of the cornea, owing to gravity and the tight fit of the upper lid [15]. (8) Undue prolongation of conjunctivitis following minor corneal injury.

CLASSIFICATION OF USUAL CAUSES (WITH SPECIAL CHARACTERISTICS)

(A) *Direct trauma.*—Rubbing with saliva-covered finger, match head, pencil (copying ink). Tendency to subconjunctival hæmorrhage.

(B) *Local vegetable irritants.*—Mustard, tobacco, snuff, pepper. Particles tend to "string" themselves on threads of mucus. The Chinese use tobacco as an eye treatment.

Cosse and Delord [5] claim that effects of tobacco, snuff and pepper are similar to ipecacuanha. I find tobacco and snuff produce considerable discharge without much œdema.

Ipecacuanha (peculiar to French-speaking armies).

Acute variety (B).—Acute, glossy, pale chemosis (due to emetine) without keratitis. Onset twelve hours after insertion, subsides in three days [8] to three weeks [4]. *Chronic variety* (from repetition) (B). Eczema of lids. Lower conjunctiva looks like lean ham or spring catarrh. Finely granular pseudo-trachomatous appearance of upper lid [3].

(C) *Oriental vegetable irritants.*—Pulp of jequirity, croton and castor oil seeds: Native troops in the British Army in India [6]. Acute chemosis with small central area of. necrosis leading to a local symblepharon.

(D) *Unorganized deposits.*—Soot (as solid or straw smoke [2]), slack coal, dust, earth. and cigarette ash: May be found in one lower fornix only, as, being only slightly irritant, they are often inserted just before examination. Must be differentiated from airborne dust which adheres in great amounts to any blob of pus at inner canthus, but only gets into lower fornix in high wind or filthy atmosphere. The injection produced is brighter red than that due to group B.

(E) *Calcium salts.* $Ca(OH)_2$, $CaSO_4$.—Heavy corneal scarring with a petrifying incrustation of the lashes has been observed from mortar [13] and a conjunctivitis has been produced by toothpaste, the features of which, except that it is both severe and chronic, are unknown to me.

(F) *Soap* is indetectable microscopically, and even in quantity is difficult to identify for forensic purposes unless it contains carbolic acid (Roche Lynch). As normal pH of the tears is 7·8 and household soap is alkaline, British Drug Houses phenol red paper (pH 6·8 to 8·4) which is yellow or faintly pink, in normal tears, might be used to detect recent insertion. Catarrhal inflammation, particularly rosacea, seems to increase the pH a little. Tintometric methods are useless, as the proteins and variable CO_2 content of tears prevent an accurate estimate, and good toilet soap is neutral. A slip of old dry soap may even be acid.

(G) *Fluids*.—Urine, petrol, zinc chloride (killed spirit), Odo-Ro-No [16] whose composition is not listed in Martindale but probably like most deodorants contains beta-naphthol.

Signs of the above type, although they indicate probabilities rather than certainties, may be so clear that the surgeon and military or legal authority are convinced.

In other cases where the signs are not clear-cut, to avoid injustice a confirmation by concealed observation or confession may be necessary. As malingerers do not as a rule wish to blind even one eye permanently, an explanation of the serious condition of the eye, plus a query regarding a self-applied "treatment" may elicit a confession; sometimes direct questioning is enough.

If not, the following methods of examination may clarify matters:

(1) To exclude natural causes: (*a*) Syringing of lacrimal sac; (*b*) consideration of over-treatment (a patch test): (*c*) exposure of upper fornix (Terson's method [12]).

(2) Examination of conjunctival smear: Bollack [6] found a marked eosinophilia in the discharge of ten cases of chronic conjunctivitis artefacta. Unfortunately although this is only found naturally in pemphigus, spring catarrh, and the rare "necrotic staphylococcal" conjunctivitis, it may not help much, as it may be peculiar to the rare variety due to ipecacuanha. One of Bollack's cases was of this nature, another caused by an unspecified insecticide, and the other eight were uncertain though probably due to ipecacuanha also. I have never used this test myself.

(3) Culture of conjunctival sac is alleged to be negative in ipecacuanha cases, and frequently so in others. I have found that streptococci or mixed secondary infection may occur in artefacts due to dust and tobacco.

(4) Occlusive collodion bandage: I have heard senior colleagues describe this measure as impractical, and it is useful only as an in-patient measure, where it can be watched. A small pad only should be put over the eye, with several layers of collodion-soaked gauze to follow. Special care should be paid to the upper nasal edge, where it is liable to separate, and the surfaces for adhesion are narrow. Blegvad has suggested a mask like the old "P.H." helmet (used in the last war as an antidote to phosgene), with watchglass eyepieces, and an opening for the mouth only. Where continuous observation is not possible, Wright has suggested a tarsorrhaphy complete except for 2 mm. at either end. It is possible that thermoplastic methylacrylate may solve the mechanical side of this problem.

Clinically, if the eye is irrigated before application, the bandage may cure the eye in three days. If secondary infection is well established, this may be exacerbated, and cloud the issue.

(5) Search of belongings on admission including purse, back of watch, steel helmet lining.

(6) Microscopic examination for irritants: This is an adjunct only to other clinical methods, and effective only in cases due to causes in groups B, D and E. It is rapid, applicable at the first examination, and a positive finding is conclusive. It is not so effective as analogy with detective stories might suggest, and I have under my care at this moment three cases about which I still have doubts, after doing all these tests. I have solved five cases in the past year, however, by its aid.

Persistence of detectable deposit.—I have no accurate information on this point, but have found excessive coal-dust deposit three days after, and fine wood dust two days after exposure in "naturally" inflamed eyes. In an artificial case the deposit is heavier, and as Caiger [11] has indicated, may be renewed by the patient as the effects may be transient. If nothing is found at the first examination, and the eye is recovering: (1) Give warning via a subordinate of a "special" examination, next day. (2) Do not irrigate the eye prior to examination. (3) After remarking that the eye is looking better, leave the patient alone in the middle of the examination, after insertion of a drop of saline to "dilate the pupil".

Collection of discharge.—Technique A: Stiff slightly roughened platinum loop, in collapsible holder, slide in box, and small spirit lamp, should always be carried, as they may be needed at first examination, if suspicions are aroused. At least three blobs of of mucus should be put on a slide, from which all dust has been removed by flaming or careful polishing. Different specimens can be selected under slit-lamp by direct vision, and examined in the next few hours.

Technique B: Rubbing the lid lining with pinshead of absorbent cotton-wool of pyroxylin in forceps may have value when the powder is almost dispersed, but it is difficult to see the powder through the cotton-wool, and more difficult to dissolve pyroxylin in a mixture of ether (1 pt.) and alcohol (2 pts.) than is suggested by Kalt. Gun cotton (cellulose hexanitrate) is quite insoluble. A minor modification [14], where cotton-wool is put in a watch-glass of water, and dust is collected with an eye-dropper from the upper and lower surfaces of the fluid, has been suggested by Locard.

Technique C: Centrifugalize with Na_2CO_3 to dissolve mucin, wash and examine residue. (Suggested by Professor McLeod, but not yet tried.)

Staining examination.—(1) Add a drop of water and coverslip. Add 2% NaOH to reduce mucin if very thick. (2) Lugol's iodine drawn under with blotting-paper half-way to get requisite graduated dilution. (Stains starch blue). (3) Phloroglucin (1·5% aqueous) after half a minute conc. HCl. (Stains ligneous material red.) (4) Dilute sodium hypochlorite, 3 mins., wash, iodine green 5 mins. (Stains cell walls.)

Examine these at once, as they will not keep. Compare with permanent specimens or photomicrographs. The iodine green method should be reserved if pepper is suspected, but the others are generally applicable to vegetable material.

Permanent specimens for comparison.—Most of these have been prepared and photographed by putting on the powder a drop of melted gelatine-glycerine, and a coverslip on a slide. Where iodine or phloroglucin has been used, photographs have been taken immediately. These photographs and their analysis are the original part of this paper. They were produced because the verbal description in other papers left one in some doubt on examining actual cases.

MICROSCOPY OF DEPOSITS

Vegetable irritants (figs. A1, 2 and 3).—Mustard: This consists of ground-up seeds, and flour, but is sold as a mixed substance, and some of the unstained fresh preparations contain bright yellow patches, which may be colouring matter.

Transparent cells are visible filled with starch grains, and with a certain amount of starch around them.

Pepper: This is ground-up peppercorn, and consists of masses of yellow thick-walled elongated cells, which may be found separately or clumped together—rather like a honeycomb. The cells contain round balls of starch grains, which are shown stained by iodine. Little of the so-called external striation mentioned by Kalt is visible. With phloroglucin a little non-characteristic tracheid wood can be seen.

Ipecacuanha: It is very difficult to find anything characteristic in this material. Occasionally woody bundles, or tracheids staining yellow with iodine, and red with phloroglucin, can be found. Kalt [1] in actual practice was never able to find traces of wood, and relies upon the smallness of the starch grains, which are unique, for identification.

The only other starch in ordinary use with grains as small as this is rice. As this has been used in face-powder, there might be confusion in a female case, but several face-powders tested recently give no reaction with iodine, so that some other substance may have been substituted instead of rice.

As the picture here is of pulv. ipecac. co. which contains opium and glucose, the crystals which slowly dissolve in water are probably glucose (*see* fig. A2).

Tobacco (pipe, cigarette, and snuff) (figs. B1, 2 and 3).—Cosse and Delord find that except for its brown colour, and lack of starch, which are the result of fermentation during treatment, the grains of tobacco found in the eyes of malingerers are those of the solanaceæ in general (which include belladonna and the potato plant), i.e. the leaves contain veins and tracheids of woody material (which stain with phloroglucin), stomata, and sand cells which contain oxalates. The surface of the leaf is characterized by simple and glandular hairs, which contain essential oil. This picture is well illustrated in Kissling's *Handbuch der Tabakkunde.* In practice it is misleading as the malingerer

A3.—Pepper, × 200. Thick-walled cells showing "honey-comb" effect, and containing small starch grains. Cell in bottom left-hand corner shows these aggregated into balls inside the cell.

A2.—Pulv. ipecac. co., × 150. Showing glucose crystals and very small aggregated starch grains. Typical piece showing woody elements on the left.

A1.—Mustard, × 150. Rounded masses containing starch and seen in thin-walled cells.

B3.—Dust from cigarette tobacco. × 200. Showing sharply cut edge and leaf tracheid.

B2.—Cigarette tobacco. × 200. Showing the bigger vein from a leaf composed of tracheids (*below*) and less marked veining in leaf, together with air bubbles (*above*).

B1.—Pipe tobacco. × 113. Showing surface hairs.

C3.—Ignited soot deposit. × 150. Showing sharp-edged fragments of silica.
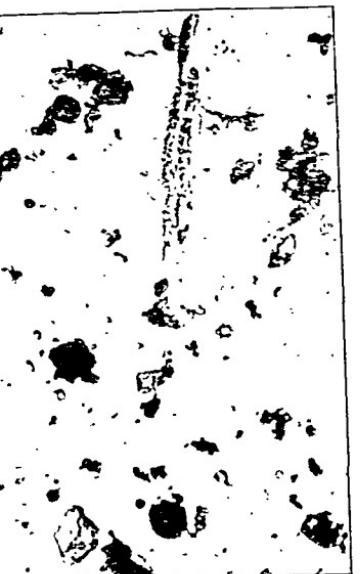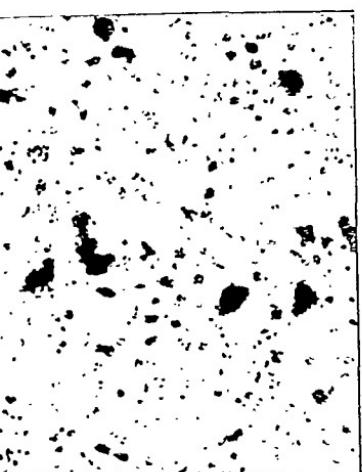
C2.—Soot. × 200. Smallest particles look like circles, being below the limits of resolution of the microscope.

These three elements make up the major portion of the ocular residue described as "ophthalmorrhyposis."

C1.—Slack coal. × 200.

E.—Toothpaste. Showing crystals of chalk under high magnification. × 985. The crystalline appearance is detectable at × 200.
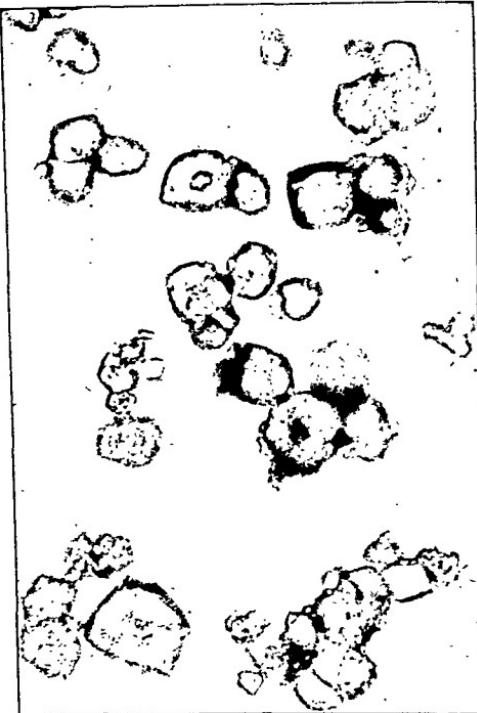
D.—Cigarette ash. × 150. The central striated area is black and the background greyish-white deposit.

B3.—Dust from cigarette tobacco. × 200. Showing sharply cut edge and leaf tracheid.

B2.—Cigarette tobacco. × 200. Showing the bigger vein from a leaf composed of tracheids (*below*) and less marked veining in leaf, together with air bubbles (*above*).
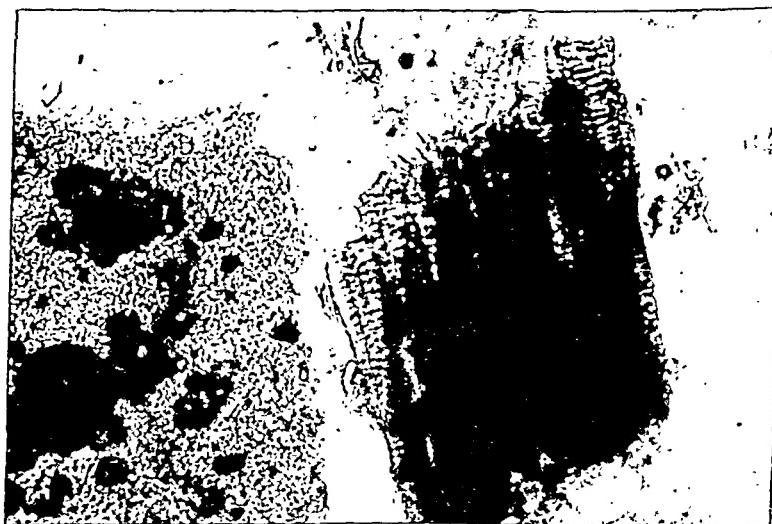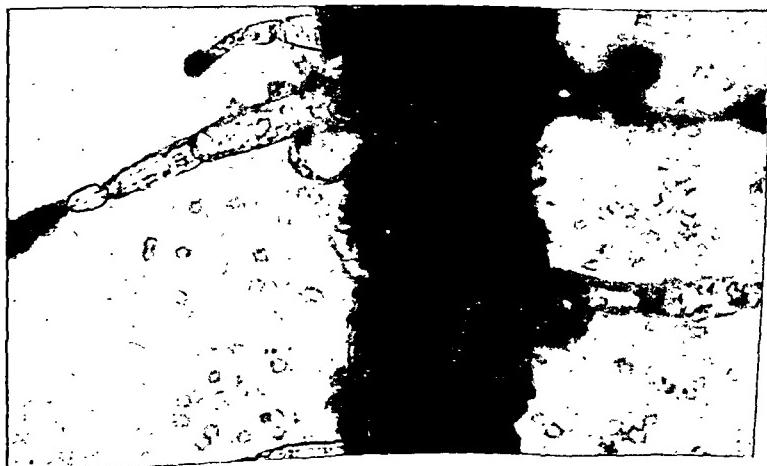
B1.—Pipe tobacco. × 113. Showing surface hairs.

In "slaked lime" the crystals are similar. Plaster of Paris contains larger chip-like crystals.

Final microscopic confirmation.—A microscopic examination of the scrapings from underneath the nail of the forefinger and thumb of the right hand, can be made (in a right-handed patient), as powders are usually introduced in this way.

This paper has necessitated the most varied inquiries and help from different experts, and I would like to express my thanks to Mr. B. Millard, Dr. B. C. Sharman, Dr. Johnstone Jervis, M.O.H. of Leeds and the City analyst, Mr. G. H. Manley, Professor Whytlaw-Gray, Dr. Roche Lynch (the Home Office analyst), Sir Norman Kendal (Head of the C.I.D.) and his officers, and to Dr. S. S. Freedman (lately my registrar) for their assistance.

REFERENCES

1 KALT, M., *Ann. oculist, Paris*, 1916, 153, 245.
2 AUBINEAU, E., *Ann. oculist, Paris*, 1916, 153, 349.
3 FROMAGET, C., and HARRIET, *Ann. oculist, Paris*, 1916, 153, 388.
4 VAN SCHEVENSTEEN, A., *Clin. ophtal.*, 1915-1916, 21, 595; also in English: *Amer. J. Ophthal.*,1917, 34, 112.
5 COSSE and DELORD, *Ann. oculist, Paris*, 1917, 154, 152.
6 BOLLACK, J., *Pr. méd.*, 1917, 25, 3.
7 RASQUIN, E., *Arch. méd. belges*, 1917, 70, 321.
8 McPHERSON, G., and DOYNE, P. G., *Brit. J. Ophthal.*, 1919, 3, 313.
9 FRIEDENWALD, H., *Amer. J. Ophthal.*, 1920, 3, 858.
10 DANIS, M., *Amer. J. Ophthal.*, 1920, 3, 601.
11 CAIGER, H., *Brit. med. J.*, 1922 (ii), 1264.
12 TERSON, A., *Ann. oculist, Paris*, 1923, 160, 483.
13 CHAILLOUS, J., *Bull. Soc. Ophtal., Paris*, 1929, 287.
14 LOCARD, E., *Traité de Criminalistique*, 1931, 2, 830.
15 OLAH, E., *Amer. J. Ophthal.*, 1932, 15, 510.
16 BLEGVAD, O., and MOLLER, H. U., *Acta ophthal., Kbh.*, 1935, 13, 101.
17 DUQUENOIS, P., *Ann. Méd. Lég.*, 1938, 18, 104.
18 WRIGHT, R. E., Personal Communication, 1943.

Lieut.-Colonel R. E. Wright said his experience was concerned with irritant remedies as a cause of blindness in the East rather than the self-inflicted conjunctivitis due to irritants defined by the title of Mr. Foster's paper.

We think of two varieties of self-inflicted injuries: Those produced deliberately with intent to evade duty such as occur in malingerers in the Forces or civil life, and those produced because of some underlying psychogenic affection. These have much in common, but neither offers clinical criteria. The malingerer's lesion is frequently one of the lower fornix on one side. One may identify the irritant in situ, or base diagnosis on a localized lesion, its appearance, the type of individual exhibiting it, and intuition; a suspicious history may help. In the Madras hospital "policeman's eye" was diagnosed offhand in Government employees for the most part correctly. Seldom had one to use detective methods. The diagnosis was affirmed and suitable treatment adopted, e.g. pencilling the upper palpebral conjunctiva with 2% silver nitrate. This frequently answered, the patient considering the treatment too great a price to pay. The malingering soldier may require an occlusive bandage. If the cornea is not involved—it seldom is in malingerers—and infection excluded, one may occlude the eye for some days, placing a suitable ointment in the fornix. The eye-pad may be fixed to the circumorbital skin with collodium flexile. A plaster of Paris bandage over a well-padded and bandaged eye can be split behind, removed and refastened any time after setting. The response of the conjunctiva to an irritant varies with the individual. All the appearances of a conjunctivitis artefacta may be produced by a coagulum of 10% protargol. Slaked lime as used by betel chewers in India, portions of chewed tobacco, or anti-gas ointment may only produce a red velvety fornix. Identification of irritants is best left to a chemist with forensic experience. Quicklime produces a violent reaction with conjunctival (and maybe corneal) necrosis. He had seen total hypopyon after a quicklime fornix injury without direct corneal damage. A localized eschar or croupous membrane, on the apposed surfaces of the lower fornix may be suggestive of conjunctivitis artefacta. In such cases one should exclude a Klebs-Löffler or other virulent infection. A bacteriologist should always be consulted, he may identify an unexpected organism indicating the method of infection.

Excretions may enter the eye deliberately or accidentally. Certain lower fornix eschars and croupous lesions cannot be identified as self-inflicted, even when exhaustive bacteriological investigation proves negative, and microscopy reveals merely eosinophilia with uncharacteristic granulation tissue. These obscure pseudomembranous lesions tend to have sequelæ like conjunctival burns. Their surface healing is accompanied by subconjunctival solid œdema, deep fibrous tissue formation, late shrinkage, pocket formation, symblepharon, and sometimes the eventual picture of so-called essential shrinkage. This leads towards a more complex field, the chronic granulomata, outside the subject under discussion.

In psychoneurotics the upper conjunctiva is sometimes the seat of election and the foreign substance perhaps oftener less irritant in type.

Major E. F. King said he felt very much disturbed by Mr. Foster's paper. It seemed that he must have been missing a number of these cases. He had been dealing with Service cases for three years and had been struck by the very great rarity of cases which even aroused suspicion. It was true that he had not carried out all these investigations, which called

utilizes the dust from a pipe-tobacco pouch, or cigarette case, and, while the description is true for the former, it is not for the latter. Owing to machining in a dry state the hairs are often completely absent from cigarette tobacco fragments, or if present, are simple and sparse. Although these hairs contain essential oils, the Imperial Tobacco Company tell me that their loss is unlikely to affect the flavour of the tobacco but they express no opinion regarding toxicity. Oxalate cells are equally rare. The woody tracheids and veins stain well with phloroglucin, and the cell protoplasm stains a dark brown with iodine. The main distinction from any other leaves, therefore, is the sharp or even parallel edges due to the cutting machine, which are occasionally found. In snuff, which is more finely ground, one can occasionally identify a piece of leaf of tobacco colour with a vein in it, but there is nothing otherwise distinctive.

Unorganized deposits (figs. *C*1, 2 and 3).—It is possible to identify by microscope in the airborne deposit contained by the blob of mucus at the inner canthus, particles of coal, soot, brownish siliceous material, and occasional pieces of straw and horse dung. The constituents vary in proportion with the domicile and recent movement. They are always present in some degree, and form a background together with globules of mucin to the other substances inserted.

A great deal of the deposit is unidentifiable, and the only clue to malicious introduction may be its distribution in the inferior fornix. The deposit is usually limited to the mucous "flytrap" at the inner canthus. Except after exposure to a high wind or unusually filthy atmosphere, it is rare to find it in the fornix itself.

Vertical illumination may facilitate microscopy, as the deposit is largely opaque, but microscopes of this type are rare. Generally speaking, for unorganized deposits chemical analysis is more effective than microscopic [17], but even when all methods (including spectroscopy) are employed, it may not be possible to state the sources of a given specimen.

Roche Lynch states that unless some unusual substance of a mineral or vegetable nature is common to two specimens of dust it is not possible to show that they have a common source: a sad contrast to the impression gained from detective stories.

The microscopic appearance of the deposits is as follows: Slack oil (*C*1): This is found in considerable quantity in the eyes of the inhabitants of mining districts, or people who wait in railway stations on a journey. It consists of metallic pointed opaque, occasionally semi-transparent, particles, which tend to be brownish and iso-diametric. Sometimes a metallic fracture is visible.

Soot (*C*2) consists of various sized aggregates composed of iso-diametric particles, which when separated from one another are characterized by the extreme fineness down to which they range.

Airborne dust ("Ophthalmorrhyposis", from $\rho\iota\pi\delta\omega$ "I befoul"): In a city like Leeds almost all eyes contain quantities of both the above substances, together with occasional vegetable debris, like straw. There are also visible brownish semi-transparent irregular sharp-edged pieces of siliceous deposit, which tend to be covered with absorbed soot. When these are separated by ignition, they are recognizable as silica. In the original state they resemble vegetation until treated with hydrochloric acid, in which they are insoluble (*C*3).

Fig. *C*3 shows rain-gauge deposits, obtained originally by an atmospheric deposition, on a high roof, and secondly after ignition, leaving the silica with occasional pieces of ferruginous material. It seems possible that this deposit may be responsible for the popularity of, and daily use of advertised eye lotions.

House dust (deposited on paper in a drawer): This appears to consist mainly of textile fibres; in this case the specimen is multicoloured, having originated in a carpet. In one case, a patient who used various means to produce conjunctivitis, introduced two pieces of coloured fibre of this type with the dust. (Slide not reproduced.)

Earth: This contains, as a rule, less soot and coal than airborne dust. It, of course, provides particularly in the country, a good deal of the siliceous portion of airborne dust, which in cities comes from the friction of traffic on the roads. Its composition naturally varies to a certain extent with the locality, but there are very few characteristic features.

Cigarette ash (fig. *D*): This displays a pattern of black fibres probably from the veins of the tobacco leaves, and greyish amorphous ash.

Calcium salts (including toothpaste) (fig. *E*).—The picture shown is of toothpaste under the high magnification of × 985. The crystals have been identified as calcite hexahydrate, by Professor Whytlaw-Gray.

Section of Neurology

President—Brigadier HUGH CAIRNS

[*November* 18, 1943]

Gunshot Wounds of the Head in the Acute Stage

(A Review of the Work of the Neurosurgical Units of the British Army)

PRESIDENT'S ADDRESS

By HUGH CAIRNS, D.M., F.R.C.S.

(*Consultant Neurosurgeon to the Army at Home*)

ABSTRACT, together with some notes on the use of penicillin in gunshot
wounds of the head. (Full paper appeared in *Brit. med. J.*, 1944 (i), 33.)

(1) The treatment of gunshot wounds of the head by Neurosurgical Units of the
British Army in Middle East and North Africa was described.

(2) Three units treated 459 non-penetrating head injuries (wounds of the scalp and
skull with dura intact), with 3 deaths.

(3) There were 506 penetrating brain injuries, with 83 deaths. The variation of mor-
tality in the different series depended largely on the level on the lines of communication
at which each unit was working.

(4) In penetrating brain wounds, when debridement was incomplete, or performed late,
about 25% of those who survived the immediate effects of brain injury subsequently
developed brain abscess. The onset of intracranial infection occurred later than in the
case of the 1914-1918 war and a considerable proportion recovered with further treat-
ment.

(5) At the C.C.S. level 28% of head wounds were complicated by wounds in other
parts of the body. Non-penetrating head wounds were twice as frequent as brain wounds.
The mortality for brain wounds was about 25%. In "fresh" cases operated on by neuro-
surgeons the incidence of post-operative intracranial infection was minimal (3·7%).

(6) Of 36 head wounds three to twelve days old all but one were found to contain
bacteria. The predominating infecting organism was *Staphylococcus aureus* (23 cases).
Evidence was obtained that in the majority of brain wounds infection develops in the
superficial layers of the wound and spreads thence to the deeper layers.

(7) *Penicillin.*—With the help of Professor Florey a trial was made by Neurosurgical
Units at Tripoli and Sousse of penicillin applied locally to brain wounds of the Battle of
Sicily. Wounds three days old or older were chosen, because there were not enough cases
to do alternate cases, and Eden's earlier work had shown that the results of operation
on recent wounds by current methods were very good. The method employed was to
excise and suture the wound as before. Before the wound was closed a fine rubber tube
was led through a stab-hole into the brain cavity and calcium penicillin solution (250 units
per c.c.) was injected into the cavity twice daily for four to five days. The average
amount used was 15,000 units per case, but in future cases the total dose would probably
be smaller. Before each injection the contents of the brain wound were aspirated.

During the battle 25 cases of penetrating brain wounds three to twelve days old were
admitted. Two were moribund on arrival, with large brain fungus; these were not opera-
ted on and they died shortly after admission. Of the 23 wounds three to twelve days old,
13 were at the time of operation to the naked eye purulent, some with pus under the
scalp or in the temporal muscle, others with pus in the brain and in the superficial
layers. Four of the wounds presented a brain fungus. Nineteen of the 22 cases examined
were shown to be infected with Gram-positive pyogens. All these wounds—purulent as
well as non-purulent—were closed completely, except one in which there was so much
skin loss that it was only possible to close part of the wound.

This work is reported in detail elsewhere (Cairns, Eden and Shoreston, 1943, "Preliminary
Report to the War Office and the Medical Research Council on Investigations Concerning

for the skill of a detective, a chemist, and a psychiatrist, as well as an ophthalmologist. He thought that he had seen only six or eight suspicious cases and always he had found some difficulty in clinching the diagnosis. With regard to the psychological element, he agreed with Colonel Wright that there was the frank malingerer who was fairly easily detected. In addition to the malingerer and the psychoneurotic there was a third group, namely, the half-wit, who, under modern conditions, found himself left behind. He had seen one such case with a self-inflicted conjunctivitis.

There was a condition of the cornea which he had found to be helpful in these cases; namely, in the lower third of the cornea a curious punctate drying of the epithelium. This was quite sharply confined to the area stated, and was obviously an effect of irritation from the outside.

With regard to occlusion of one eye with a shield or by some other method, this always seemed to raise its own problems. The ventilation of the eye was interfered with, which in itself led to a certain amount of irritation.

Mr. Humphrey Neame said that there had been no great emphasis on the right- or left-handedness of these persons. It was worth while in suspicious cases testing whether the person was right-handed and right-eyed. He recalled one case in which the left eye was maltreated, and the person was left-handed. He was quite convinced from the appearance that this was an artefact.

Mr. Frederick Ridley said that he had a case similar to that described by Major King, which also showed fine superficial staining of the lower half of the cornea. He was almost sure the patient was a malingerer. This staining might prove to be of real diagnostic importance. He wondered whether Mr. Foster had thought of the use of sodium alginate to pick up and fix fine dust or other material introduced into the conjunctival sac. The sodium salt was precipitated as calcium alginate and the tough jelly so formed was a suitable embedding material for subsequent staining and microscopic examination. A kallodent mask was easily made and was an effective shield if tied above and below the ears and the knot sealed.

Mr. Foster, in replying, said that he regretted he did not know anything about sodium alginate nor had the relationship between right- and left-handedness come within his purview. By analogy with skin diseases there might easily be some relationship between handedness and the inflamed eye.

Clinical Experiences with a R.C.A.M.C. Neuropsychiatric Division in England 1940 to 1944

By Lieutenant-Colonel J. CLIFFORD RICHARDSON, M.B.E., R.C.A.M.C.

IT is my purpose here merely to report in a condensed form some facts and impressions based on three and a half years' service with the Canadian Neurological Hospital in England. The hospital consists of a surgical division which is neurosurgical and of a medical division which is neurological and psychiatric. This report is based entirely on the "neuropsychiatric" division.

DEVELOPMENT

In 1940 a two hundred bed special field hospital was planned with the primary purpose of treating head injuries and battle neuroses near the forward area. Because of the fall of France while the hospital was on the way to this country, it settled in England and has since dealt chiefly with casualties from this large overseas base rather than battle casualties in the field. It enlarged gradually in bed space and personnel and by July 1943 reached its present status as a 600 bed hospital. In that is included a Plastic Surgery Unit of 150 beds so that the neurological hospital actually has 450 beds. The neuropsychiatric division has an arbitrary 250 beds. The progressive enlargement of this hospital unit was paralleled by an even more rapid expansion of the whole neuropsychiatric services of the Canadian Army Overseas. A consultant was appointed in London to perform the consulting and advisory duties which had been done in a much smaller scale by the hospital staff. An increasing number of regional neuropsychiatric specialists were sent out to field medical units, general hospitals and to special duties such as liaison with the Personnel Selection Branch, with the Officer Selection Centre, with a Reallocation Centre, and with special companies for unstable and mentally dull soldiers. All of these trained specialists spent at least two months with the hospital so that it has retained a nuclear position in the whole Service.

For two years an attempt has been made to disseminate and standardize knowledge of military neuropsychiatry throughout the general hospitals. For that purpose at least one physician from each general hospital has been attached to our division for periods of one to three months. Our professional staff has been a constantly changing one which has provided many ideas and points of view though it has handicapped the continuity of investigation.

The case material of the division in its first three years has beeen analysed in the broad classification shown in the table. It is based on discharges rather than admissions so that it does not include several cases which were transferred to the neurosurgical division for operative treatment. It should be emphasized, too, that the admissions to the surgical division are not included. The vast majority of the patients were Canadian soldiers but there have also been included R.C.A.F. personnel, and a few from the Canadian Navy, civilians and British Services. Of the 4,426 cases it is seen that 3,084 or 70% were mild or severe mental disorders; 828 or 19% were "neurological" diseases without prominent mental disturbances; 8% were general medical diseases and 3% were cases in which no abnormality was detected.

The *psychoneuroses* comprise the largest group. Only a few could be termed battle casualties and many were life-long "constitutional" neurotics. Very few of these patients, surveyed during this period, had experienced any significant battle stress. The group called *psychopaths* is a large one comprised of a variety of social misfits, often presented to us under close arrest for opinion about medico-legal aspects as well as decision about military fitness. The cases of *pre-psychotic personality* have been included with the psychopaths for simplification though with our more recent standards of nomenclature we now classify them in a separate group. *Drug and alcohol addiction* also warrant separate grouping in our present nomenclature. Only three patients were labelled as malingerers. Two of these were court-martialled and convicted. The third proved to be a mistake; a very capable medical officer ventured this opinion at the time with slight qualification; eighteen months later the patient returned to hospital with indubitable signs of spastic paraplegia. *Psychoses* of all types have been encountered, even one case of senile dementia. Confusional states related to exhaustion and infections from an interesting small group. There were four cases of toxic psychosis with atypical pneumonia.

the Use of Penicillin in War Wounds", p. 97, War Office, A.M.D.7/90D/43, London). By regular examination of the aspirated fluid we found that Gram-positive organisms disappeared after two days' treatment, in all except 2 cases. In all cases Gram-negatives— pyocyaneus, proteus and coli—persisted, usually until the discharge through tube or drainage hole ceased. If the wounds gaped at any point, as sometimes after a week they did, *Staph. aureus* could occasionally be grown again from the raw surface, but did not appear to interfere with healing.

Three of these 23 patients died—one from an intracerebral clot, and the other two from infection. One of these had a severely infected eight-day-old left frontal wound with a brain fungus, and in the left frontal lobe indriven bone fragments and 3 different brain abscesses from which pneumococcus was grown. He died about forty-eight hours after operation of spreading cerebral œdema, and at necropsy still had pneumococci in the abscess wall. Penicillin did not get a long enough application in this case. Possibly it would have been better to have treated him expectantly for a few days, as the Germans have recommended for brain wounds of this age (Tönnis, W., 1941, *Zbl. Neurochir.*, 6, 113). but with the addition of local and parenteral sodium penicillin.

The other case was a man with an eight-day-old right frontal wound infected with *Staph. aureus*, whose pus became Gram-negative under penicillin treatment (in addition to calcium penicillin, applied locally to the brain wound, he had sodium penicillin, 485,000 units, intramuscularly because of a compound fracture of the femur). This man became drowsy and died on the tenth day after operation, and at necropsy was found to have an abscess in his right frontal lobe which had been incompletely tapped during the last days of his illness. This case is a failure of surgical technique, and it shows the importance of maintaining drainage during penicillin treatment.

Wound healing in the 20 survivors, observed for not less than three weeks in all but 5 cases. The healing was by first intention in 6 cases. In 13 there was a slight gape or sinus in the wound, usually at the site of greatest tension, but most of the wound healed by first intention. These gapes were usually not serious, for only in one case did a small fungus appear during healing.

These results compare favourably with other series of wounds of similar age, especially when we consider that more than half of the wounds were purulent and would not hitherto have been sewn up. But the series is small and has not yet been followed for more than 62 days. Brain abscess might still appear in some.

During the Battle of Sicily the opportunity also presented of treating 17 cases of non-penetrating wounds, one and a half to sixteen days old, locally with pencillin, usually as a solution, sometimes in powdered form. The older cases were heavily infected, with fractures of the skull and bare bone lying at the bottom of a suppurating granulating wound. These wounds and the underlying skull were excised and sutured, and all except two healed satisfactorily, though certain technical mistakes were made at first and temporary sinus formation was not uncommon. In these cases the bacteriological results were not so satisfactory as in the penetrating wounds: in a number the purulent discharge from the sinus continued to show Gram-positive organisms, and these were with one exception cases in which the skull had been fractured. Penicillin is so sure in its effects on Gram-positive cocci, apart from the occasional penicillin-resistant strain, that it is reasonably certain that the solution did not reach all the infected parts. The assumption may be made that there were small foci of osteomyelitis beyond the margin of excised bone. In gunshot wounds exposing and perhaps breaking the skull it is unlikely, when surgical treatment is not immediately available, that good healing will be obtained unless the exposed (and probably infected) bone is very widely excised.

Professor Geoffrey Jefferson: One of the causes for the lowered mortality rates in the present war is the excellent, if small, supply of well-trained young neurosurgeons; another factor, our progress in antiseptic chemotherapy. The vastly improved surgical equipment and the stationing of experts at strategical points are a tremendous advance. In the last war there was no plan for neurosurgery; such arrangements as were made were local and in a sense fortuitous (e.g. the centres of Adie and Wagstaffe, of Sargent and Holmes, and my own).[1] Of the instrumentation the most important seems to be really adequate suction; this was inadequate in the last war. The President's foresight and his persuasive powers induced the War Office to provide powered trucks capable of generating current for diathermy and electrical suction in the desert. There is, however, another important issue which arises because of the relative fewness of specialists. In spite of the best of planning 20% of head wounds (and often more) have to be cared for by general surgeons. I have always pleaded for the training of skilful general surgeons in the methods of modern neurosurgery at the Special Centres in Britain. They learn extremely fast and I am sure that we could do more of this valuable teaching if more surgeons were sent for short courses.

[1] The bacteriology of my own cases in the last war was recorded in my paper. Anaerobes were frequent, but gas infection of the brain was not a serious problem. An illustration of it was reproduced in my 1919 paper (*Brit. J. Surg.*, 1919, 7, 268, 285).

ORGANIZATION AND METHODS

These have developed as needed by the number and nature of the case material, and to fulfil the needs of teaching medical officers. Until the division acquired its present enlarged complement of wards and medical officers six months ago, the neuroses and organic neurological cases were mixed in open wards and only the psychoses and aggressive psychopaths were segregated. Such an organization proved satisfactory for investigation and disposal of cases and had certain advantages in simplifying administration and in promoting a uniform psychic and somatic approach to both types of cases. The admixture of neuroses and neurological diseases did, however, handicap our attempts to arrange active treatment and rehabilitation of neuroses and was not fully satisfactory for teaching. In July 1943 when facilities became available the division was reorganized with greater segregation of cases.

Neuropsychiatric Division, R.C.A.M.C.

This scheme has continued to the present and is illustrated by the diagram. The seven wards of the division have been allotted to three units: one two-ward unit of 68 beds is devoted to organic neurology, the second three-ward unit of 96 beds is for psychoneuroses and the third unit consists of two closed wards, 72 beds, for psychotics and psychopaths. Officer accommodation is separate.

The two neurological wards are always well supplied with cases and their organization requires no special comment. Highly important in the satisfactory functioning of this unit are the liaison with neurosurgery and the assistance of the radiologist and pathologist. Electro-encephalography has been done for us by Wing-Commander Denis Williams. Ward rounds, consultations, and clinical meetings with the neurosurgeons provide the teaching adjuncts.

In the two closed wards the psychotics and psychopaths are segregated as much as possible. The psychotics are repatriated within short periods (one to two months). Therapeutic malaria is used for paretics and electroconvulsive therapy for depressive psychoses. Insulin shock therapy has not been employed overseas. Experience with the disciplinary problems, the misfits and the early and acute psychotics seen on these wards is a valuable part of the training available to the medical officers at the hospital.

The neurosis unit is the most important from the practical military standpoint of returning men to service. 55 to 60% of the cases have been returned to duty. In our present arrangement, the three wards of the neurosis unit are "admitting", "treatment", and "training" wards. The cases are all admitted to one ward where the necessary clinical and laboratory investigations are rapidly carried out. Within a few days the medical officer brings each new case before the daily neurosis conference, where the

Organic neurological diseases.—The largest number of cases were proven epileptics though a smaller number of unsubstantiated epilepsy "suspects" are included. Simulation of epilepsy has been extremely rare. Routine investigation of the epileptic cases has revealed a few interesting rare conditions such as tuberculoma, angioma, porencephaly and agenesis of the corpus callosum. *Neurosyphilis* of all varieties was the next most common disease. There were 27 cases of paresis and tabo-paresis, 21 cases of tabes, 30 cases of meningovascular lues and 39 asymptomatic cases. The vast majority were caused by pre-enlistment infections. The 67 cases of *sciatica* shown were cases treated medically, and not included were about 40 cases transferred to neurosurgery for operative treatment of herniated intervertebral disc. There were also many other cases admitted directly to the surgical division. Of all the cases of sciatica admitted to the hospital a careful survey has shown herniation of lumbar intervertebral discs to be much the commonest cause. The 60 cases listed as *post-traumatic* state are those in which symptoms following head injury were accepted as clearly physiogenic, but it is quite admissible that this separation from the 56 cases grouped separately as post-traumatic neurosis is not fully justified. Under *"neuritis and nerve injury"* are included cases of brachial neuritis, ulnar neuritis, nerve contusions and old nerve wounds. The cases of *polyneuritis* were most commonly of the post-diphtheritic type. There were only eight cases of acute infective polyneuritis. One of these was fatal and detailed pathological study showed it to be a pure polyradiculitis.

The remaining neurological diseases shown in the table deserve no special mention here though various isolated cases of considerable clinical interest were encountered. In the muscular diseases there were eight cases of myotonia and two cases of familial periodic paralysis. We have not seen any certain case of myasthenia gravis. It is of interest that there were only 15 cases of *disseminated sclerosis*. Though the majority of cases of neurological diseases in Canadian soldiers have been sent to this hospital, a few, particularly acute conditions, have been treated in Canadian general hospitals. Thus we have had only eight cases of *spontaneous subarachnoid hæmorrhage* and I know of about six others which have been in general hospitals. Cases of cerebrospinal meningitis and meningococcæmia have been entirely treated in general hospitals.

SUMMARY OF TOTAL DISCHARGES FROM MEDICAL DIVISION
THREE-YEAR PERIOD—SEPTEMBER 28, 1940, TO SEPTEMBER 19, 1943.

Total 4,426 Cases

PSYCHONEUROSIS (1,625)

Anxiety states	869
Psychoneurosis (unspecified)	194
Anxiety hysteria	169
Hysteria	162
Reactive depression	91
Psychosomatic diagnosis	68
Post-traumatic neurosis	56
Neurasthenia	12
Obsessional states	4

PSYCHOPATHIC PERSONALITY (646)

Antisocial and sexual types	297
Inadequate and temperamentally unstable types	243
Pre-psychotic personality	77
(Drug addiction	14)
(Alcohol addiction	12)
(Malingering	3)

PSYCHOSIS (507)

Schizophrenia	355
Manic depressive	88
Chronic alcoholism	38
Toxic psychosis	10
Organic dementia (traum. etc.)	6
Mental defect with psychosis	6
Presenile and senile	4

MENTAL DEFECT (306)

NEUROLOGICAL DISEASES (828)

|	
Epilepsy	275
Neurosyphilis	117
Sciatica	67
Post-traumatic state	60
Neuritis and N. injury	60
Polyneuritis	41
Migraine	26
Not yet diagnosed neurologically	21
Narcolepsy	19
Muscular diseases	18
Spinal cord diseases	17
Disseminated sclerosis	15
Cerebral trauma	15
Parkinsonism	13
Symptomatic diagnoses	13
Ménière's disease	11
Neurocirculatory disease	8
Subarachnoid hæmorrhage	8
Other cerebral dis.	8
Cerebral tumours	6
Cerebral hæm. and throm.	5
Meningitis and sequelæ	5

GENERAL MEDICINE (379)

Nothing abnormal diagnosed (135)

In the total cases here tabulated it is striking that the "psychiatric" disorders greatly predominate, almost four of them to one "neurological" case. This disproportion is even greater in our out-patient experience and in the consulting work of the regional neuro-psychiatric specialists. It should be emphasized, however, that the final grouping as here shown is in some degree arbitrary, due to the inevitable overlapping, and that such final diagnoses are only reached after both psychic and somatic investigations in all of the cases.

ORGANIZATION AND METHODS

These have developed as needed by the number and nature of the case material, and to fulfil the needs of teaching medical officers. Until the division acquired its present enlarged complement of wards and medical officers six months ago, the neuroses and organic neurological cases were mixed in open wards and only the psychoses and aggressive psychopaths were segregated. Such an organization proved satisfactory for investigation and disposal of cases and had certain advantages in simplifying administration and in promoting a uniform psychic and somatic approach to both types of cases. The admixture of neuroses and neurological diseases did, however, handicap our attempts to arrange active treatment and rehabilitation of neuroses and was not fully satisfactory for teaching. In July 1943 when facilities became available the division was reorganized with greater segregation of cases.

Neuropsychiatric Division, R.C.A.M.C.

This scheme has continued to the present and is illustrated by the diagram. The seven wards of the division have been allotted to three units: one two-ward unit of 68 beds is devoted to organic neurology, the second three-ward unit of 96 beds is for psychoneuroses and the third unit consists of two closed wards, 72 beds, for psychotics and psychopaths. Officer accommodation is separate.

The two neurological wards are always well supplied with cases and their organization requires no special comment. Highly important in the satisfactory functioning of this unit are the liaison with neurosurgery and the assistance of the radiologist and pathologist. Electro-encephalography has been done for us by Wing-Commander Denis Williams. Ward rounds, consultations, and clinical meetings with the neurosurgeons provide the teaching adjuncts.

In the two closed wards the psychotics and psychopaths are segregated as much as possible. The psychotics are repatriated within short periods (one to two months). Therapeutic malaria is used for paretics and electroconvulsive therapy for depressive psychoses. Insulin shock therapy has not been employed overseas. Experience with the disciplinary problems, the misfits and the early and acute psychotics seen on these wards is a valuable part of the training available to the medical officers at the hospital.

The neurosis unit is the most important from the practical military standpoint of returning men to service. 55 to 60% of the cases have been returned to duty. In our present arrangement, the three wards of the neurosis unit are "admitting", "treatment", and "training" wards. The cases are all admitted to one ward where the necessary clinical and laboratory investigations are rapidly carried out. Within a few days the medical officer brings each new case before the daily neurosis conference, where the

prognosis and treatment are the prime considerations. The hopeless chronic neurotics are "by-passed", boarded and sent out of hospital as rapidly as possible. In the remaining worth-while cases, all are given individual psychological treatment in some degree. When indicated they are sent to the "treatment" ward for continuous narcosis or modified insulin therapy. On the training and rehabilitation ward the man is handled more as a soldier than as a patient and is kept busy on a planned programme embodying physical training, sports, discussion groups, training films, handicrafts and constructive work such as farming and landscaping. This emphasis on therapy, full activity and rapid disposal of hopeless cases has certainly been facilitated by the segregation of neuroses in a unit. The medical officers attached to this unit have a concentrated experience with neuroses through the rapid turnover of patients and the frequent conferences. The plan followed in training of posted medical officers is one of rotation throughout the three different units so that equal experience is gained with all aspects of neuropsychiatry. We now have a well-trained psychologist on the hospital staff. There is wide scope for psychological assistance in various aspects of the hospital work.

The experience of the hospital has been that neurology, psychiatry and neurosurgery blend smoothly as different closely allied components of the one broad field of medical practice. The advantages of a co-operative handling of diseases of these various types in one hospital have been apparent from the viewpoints of diagnostic facilities, treatment, post-graduate training and of clinical investigation. The liaison has helped to break down artificial barriers between neurology and psychiatry.

There would be a loss of interest, economy and teaching facilities if these units of neuroses, neurological diseases and psychoses were in separate hospitals. Each of the units and the allied department of neurosurgery have many problems in common.

The expansion of neuropsychiatric services in the Canadian Army Overseas in response to needs and requests, rather than to a preconceived plan, suggests that the trend may be indicative of future developments. The military expansion has been in the two directions towards sociology and towards clinical medicine, which is comparable to public health and clinical practice in general medicine. This review of our hospital experience pertains only indirectly to the broader sociological aspects. Certainly neuropsychiatry has been called upon to play a far larger part in selection of recruits, allocation of personnel and selection of officer candidates than was originally anticipated. In our hospital work we have been in more direct contact with the general physicians and have been impressed by their greatly increased interest in the psychiatric aspects of illness.

The lamentable inadequacies of teaching of so-called "functional" illnesses to medical students has become much more evident during this war and will undoubtedly be remedied afterwards. Teaching hospitals are already planning improvements including the reorganization of departments of neuropsychiatry in their medical wings.

The opinions expressed are those of the author and are not intended as any authoritative expression of policy of the R.C.A.M.C. The organization and clinical work of the hospital division have been shared by so many that full acknowledgments here are impracticable. Colonel Colin K. Russel was largely responsible for the original formation of No. 1 Canadian Neurological Hospital. He was the first officer in charge of its medical division and was the first consultant in neuropsychiatry to the Canadian Army Overseas. Much of the work here reported was under the direction of my predecessor Lieut.-Colonel H. H. Hyland. Colonel F. H. Van Nostrand, the present overseas consultant, has been in charge of the expansion and development of the whole neuropsychiatric service.

Spinal Epidural Granuloma

By Major Wm. S. Keith, R.C.A.M.C.

This clinical report is based on two cases of staphylococcus infection involving the epidural space in the dorsal spine. In each case the patient developed a severe though incomplete paraplegia about six years after the original infection. At laminectomy the epidural fat was found to be replaced by dense tough scar tissue which occupied the dorsal half to two-thirds of the spinal canal.

Case I.—Girl, aged 6. Admitted to the Hospital for Sick Children, Toronto, in 1934, with high fever and somewhat stiff neck. Cerebrospinal fluid was normal. Pus was found in her urine and a diagnosis of pyelitis was made. A day or so later *Staphylococcus aureus* was grown in a blood culture. A second lumbar puncture a few days later estab-

lished a diagnosis of staphylococcal meningitis. She was treated with staphylococcus antitoxin intrathecally and intramuscularly and eventually recovered from the meningitis. About a month after the onset of her illness, a swelling deep in the back of the neck pointed and drained. X-ray then revealed that the original lesion was hæmatogenous osteomyelitis of the lamina and pedicle of the 5th cervical vertebra. When her general condition had greatly improved at about three months from the onset of the illness the cervical spine was exposed through the mid-line and sequestra and granulation tissue were excised. The wound failed to heal but after a further exploration with the removal of some living bone and more granulation tissue the wound eventually healed and the patient remained well.

She returned to the out-patient department about one and a half years after the onset of the infection with a discharging sinus to the right of the 7th and 8th dorsal spines. X-rays of the spine and neurological examination were negative. The sinus healed and discharged intermittently at about two to three month intervals until 1938, when it was explored. The neurological examination was negative. About 1½ in. of the 7th rib was removed close to the spinal column. A pocket of granulation tissue lying against the sides of the vertebral bodies was cleaned out and packed. No sinus or track of granulations could be located passing into the spinal canal. After another six months of intermittent discharge, this sinus finally closed and has since remained healed.

In 1941, about six years after the start of her troubles, she began to complain of difficulty in walking and stiffness of her legs. She was examined on several occasions by Dr. W. A. Hawke and me. She had a paraplegia of increasing severity with extensor plantar responses, spastic legs with increased tendon reflexes, diminished position and vibration sense and finally a definite diminution of all forms of sensation below the 6th dorsal dermatome in front. She had only slight intermittent pain around the chest. There was an incomplete spinal block and an increase in protein in the spinal fluid. She had some difficulty with urination but did not have to be catheterized.

A laminectomy was performed from D.4 to D.9 inclusive. We found that the spinal canal was filled with dense tough scar tissue which was cut into carefully for the full length and width of the exposure. When the depth of the incision in the scar seemed to be two-thirds of the depth of the spinal canal, I abandoned the operation without having identified the dura mater. Recovery was complete. In March 1942 there was no trace of sensory disturbance. She had a normal gait and flexor plantar responses.

Case II.—Female, aged 20. Early in 1937 she was admitted St. Bartholomew's Hospital where she was under the care of Mr. J. E. A. Roberts for several months. She had a staphylococcal empyema and a bronchopleural fistula. On her discharge it was stated that the primary focus of the infection seemed to be in the spine.

In 1940 she had some pain in both sides of her chest coming around under the breasts. She went to St. Mary's Hospital, Portsmouth, where X-rays of her spine and chest showed nothing abnormal. On August 10, 1943, she gave birth to her first child. Six days later on coming out of her Anderson shelter after an air raid she found that both legs dragged and were weak. She was referred to the Basingstoke Neurological and Plastic Surgery Hospital on September 8 by Doctor J. C. Prestwich and by Surgeon Rear-Admiral Rowlands.

She could adduct and flex each thigh a little but it was done slowly and with great effort. She could also invert and plantar flex the right foot slightly. The tendon reflexes were very brisk. The plantar responses were extensor. There was diminution of touch and loss of vibration, position and pain, heat and cold below the 7th dorsal dermatome in front. She had some slight intermittent pain in both sides of her chest. There was some difficulty in starting urination and she was constipated. Lumbar puncture revealed a complete block of the spinal canal on jugular compression but the spinal fluid protein was only 30 mg. There were two lymphocytes in the spinal fluid. One half cubic centimetre of lipiodol placed in the cisterna magna was arrested first at D.4 then at D.6.

A diagnosis of extradural scar was made. There was no leucocytosis or fever but we thought an abscess might have formed recently in the extradural space.

On September 10, 1943, the spinal canal was opened from the 4th to the 9th laminæ inclusive. Part of the 3rd spine and part of the 10th lamina were also removed. The pathological condition was exactly the same as in Case I except that, at the upper and lower end of the exposure, the scar was seen to thin out on to normal-looking dura. The scar tissue was incised and was then partly torn and partly cut out of the spinal canal in long strips. At one point a small pocket of granulation tissue with a bead of pus in the centre was found and excised. Scar tissue was not totally removed from the sides of the spinal canal dorsal to the roots and there were a few strips and tags of scar tissue left on the dorsal surface of the dura mater. The operation was much more thorough and satisfactory than in Case I, however. Before the wound was closed the dura had a normal "feel" throughout the whole exposure when it was palpated with a forceps or with the finger. A small drain was left in for three days. The wound healed without incident.

Twenty-four hours after operation she could move both feet with considerable freedom and she had some return of pain, heat and cold sensation. She gradually recovered until on March 18, 1944, she had the full use of her legs and was doing all her own housework. The plantar reflexes were flexor.

It is necessary to study the acute phase of this infection in order to get some light on the peculiar pathological picture which has just been described.

I have operated on only three cases of acute staphylococcal infection of the epidural space. Two were operated on for paraplegia and the third, an infant, was operated on

because thick pus was obtained at lumbar puncture although there was no paralysis. Here the whole spinal epidural space was filled with pus. In the other two cases, in addition to an epidural abscess which caused the paraplegia, there was a fairly extensive fibrino-purulent exudate in the epidural space. The infection seems to have been blood-borne to the epidural fat in each of these three cases. Wilensky (1934) gives the following description of an autopsy on a 46-year-old man who died fifteen days after the onset of a staphylococcal osteomyelitis of the 8th dorsal vertebra. The patient had had slight meningeal signs but there was no paralysis. "The spinal canal contained a large collection of stringy yellowish pus infiltrating between the dura and the vertebral column from the level of the 8th dorsal vertebra to the level of the first lumbar. The purulent process communicated through the left 8th vertebral foramen with an abscess cavity in the left costo-vertebral angle."

In Case I there was probably a purulent or fibrino-purulent exudate in most of the epidural space of the thoracic part of the spinal canal at the time she developed meningitis. This region of suppuration was never properly drained but it did gain exit from the spinal canal into the thorax and the back, probably through a lateral foramen.

In Case II the infection either entered into or escaped from the spinal canal by a similar route. The epidural suppuration again never drained properly but remained in situ for years without causing neurological symptoms.

In both cases the exudate became changed into granulation tissue and later it was gradually transformed into dense scar tissue composed of collagen fibres. The wall of the tiny abscess found in Case II was composed of lymphocytes and plasma cells. From the abscess itself no organism was grown. In Case II parturition played a part in precipitating the symptoms but in each case the proliferation and contraction of scar tissue was the primary cause of the paraplegia.

This dense tough scar tissue composed of collagen fibres and few inflammatory cells is familiar to any surgeon who has operated on cases of chronic osteomyelitis. It forms the walls of sinuses and often partly fills cavities in bone. It seems to tear or strip fairly readily.

Dandy (1926) described inflammatory tumours in the spinal epidural space. Watts and Mixter (1931) reported several cases of spinal epidural granuloma. In none of these cases did the origin of the infection seem to be more remote than two years. In a few of the cases, scar tissue was present in considerable amounts but granulation tissue composed of lymphocytes, plasma cells, polymorphonuclear cells and giant cells was the most abundant material in the formation of the tumours.

SUMMARY

Two cases are reported in which paraplegia developed about six years after a staphylococcal infection involving the spine. In each case it is probable that the spinal epidural space was the seat of a suppurative inflammation early in the course of the illness. This inflammation presumably passed through the stage of granulation tissue till it became scar tissue and finally caused the paraplegia.

In an incomplete review of the literature on this subject paraplegia occurred in all the cases in less than two years from the time of the original infection. Granuloma rather than scar tissue was the predominant pathological finding.

REFERENCES

DANDY, W. E. (1926) Abscesses and Inflammatory Tumours in the Spinal Epidural Space (So-called Pachymeningitis Externa), *Arch. Surg., Chicago*, 13, 447.
WATTS, J. W., and MIXTER, W. J. (1931) Spinal Epidural Granuloma, *New Engl. J. Med.* 204, 1335.
WILENSKY, A. O. (1934) Osteomyelitis—Its Pathogenesis, Symptomatology and Treatment. New York.

Some Aspects of the Treatment of Parkinsonism

By Major J. A. WALTERS, R.C.A.M.C.

IN 1940 the Department of Medicine of the University of Toronto required answers to several questions before a new drug could be tested in the treatment of Parkinsonism: (1) In what manner do psychological influences alter the Parkinsonian syndrome? (2) Can these factors of emotion and environment be recognized and reckoned with in any general clinical assessment of a treatment for Parkinsonism?

With this in mind a study was made during the next three years. At the Out-patient

Department of the Toronto General Hospital a series of ambulatory adult Parkinsonian patients was seen at least monthly. History and examination methods were extended to establish the general medical and neurological, the psychological or psychiatric and the social state of the patient. At the monthly visit a ten to thirty minute examination was made when variations in these states were studied and when psychotherapy, medication and advice in management were given. Patients were also visited in their homes and relatives and friends were interviewed.

Forty-seven patients were studied of whom 27 were clearly postencephalitic, 5 more were probably suffering from the late effects of encephalitis lethargica and 15 were considered to be idiopathic paralysis agitans. Several case histories well illustrate the type of evidence which indicates an important psychosomatic relationship.

Case I.—C. L., male, aged 62, had suffered paralysis agitans for five years. His main disability was tremor in four limbs, of typical pill-rolling quality in the hands and less severe in the legs. At the left wrist there was cog-wheel rigidity and at the left elbow and shoulder there was lead-pipe rigidity.

He was a machinist who was prone to worry but had had no previous neurosis or psychosis. As his tremor became evident he had developed a chronic anxiety that he would lose his job and become crippled. He did lose his job and then was sleepless, exhausted, without appetite and with more tremor. He and his wife were forced to live with a daughter-in-law who did not welcome them. He lapsed into a hopeless black mood and in desperation finally came to the hospital expecting to be pronounced incurable.

The diagnoses made were: (1) Idiopathic paralysis agitans; and (2) acute neurosis—mixed type, anxiety state and reactive depression. Treatment planned was: (1) Adequate doses of tincture of stramonium to reduce his rigidity; (2) psychotherapy to alleviate his neurosis. He needed to understand his disability, to lose his fear of crippling, to be confident of improvement without cure, and to realize that he could work usefully, enjoy life and feel better; (3) social aid to get him working and living in his own home.

Twenty-four hours after his first visit he was seen again. He was vastly better, the tremors were absent from all but the left hand where they were less. He was loud in his praises of the stramonium of which he had taken two 5-minim doses. This improvement continued. The neurosis was completely relieved, the tremor remained reduced, he felt fine and was able to work within six weeks. During this period he was taking less than 30 minims of tincture of stramonium t.d.s. and his rigidity had not lessened.

Case II.—G. W., male, aged 60, suffered from paralysis agitans for three years with typical Parkinsonian tremor in four limbs and a mild lead-pipe rigidity in the right arm. His personality was highly temperamental; he was easily discouraged and easily pleased. When well he was buoyant, energetic and sociable. When troubled he suffered depression, irascibility and worry with fatigue, headache, giddiness and nervous dyspepsia. His wife had been crippled for five years with rheumatoid arthritis and asthma. He had retired on a small pension and nursed her. Her illness had kept him in an anxiety state with nervous indigestion. When first seen in 1940 he was anxious and depressed. He disliked the tincture of stramonium which he had been taking for one year. A dose greater than 45 minims produced retching, nausea, and vomiting. On this medication he remained neurotic and our psychotherapy had no effect. Upon changing to a very small dose of Bulgarian belladonna his feeling of well-being rapidly returned, his anxiety lifting and his digestion improved. The tremor vanished from all but the right hand where it no longer embarrassed him. He became buoyant, enthusiastic and confident. He was then kept well for ten months on a placebo of a Blaud's pill, the substitution of which he remained ignorant. His health now became better than it had been for five years. His activity was not limited, he painted his cottage and he could have taken a job.

During the third year his only medication was phenobarbital gr. ¼ four times daily. His anxiety state, his indigestion and his Parkinsonian tremor all returned together for three short periods of four to six weeks. It was only then that the true sources of his varying states could be identified. His wife had begun to improve just at the time he had started to take the Bulgarian preparation. He and she remained well together until when she relapsed he again became worse. When she began to recover his health returned and his tremor subsided. His last two short relapses coincided with outbreaks of an old feud with a neighbour over a line fence. His tremor and health improved remarkably when a court decision was given in his favour.

Our study was also valuable as an attempt to assess function of the *motor system* in relation to the other human functions with which it is constantly integrated. A distinction was made between symptoms arising from affective sources and those from the deteriorated motor system. Physical signs became a matter of what the patient could and could not do at voluntary and involuntary motor levels. What could be done indicated residual psychomotor mechanisms which were still operating. What could not be done represented the sum of those mechanisms destroyed by brain damage together with those mechanisms not in operation but capable of activation if the electro-chemical state of the central nervous system could be made more normal. To the same end the other physical, psychological and social factors required repeated detailed examination to know the changing activity. Finally the total integration of these many functions in the life of a human being with individual and significant personality had to be kept

in mind. As such the study was an attempt to apply humanistic as well as scientific observations to a problem of clinical neurology. It presumed an holistic attitude throughout.

From such qualitative studies the following observations were made: (1) The health and vigour of 44 of these 47 patients were reduced by psychological and social stress which could be identified by history and examination.

(2) The unhealthy psychological states were of two main types: (*a*) *Affective states* with strong and upsetting feelings. In intensity these ranged from moderate unhappiness and worry to severe neurosis and psychosis. In quality the 32 post-encephalitic patients had eleven anxiety states and four reactive depressions. This group also had five active psychosis and ten of those paroxysmal obsessional states which are expressions of their post-encephalitic condition. The 15 paralysis agitans patients had eight anxiety states and four mixed states with anxiety and depression. One mild psychotic depression was seen. (*b*) *Personality and constitutional deterioration*: As a sequel to encephalitis 13 patients had reduced emotional control and a greater lability of feelings. In 8 patients the deterioration produced an apathetic loss of morale and they readily accepted an anergic invalidism. The paralysis agitans group, in contrast, had preserved their personalities to a greater degree. The single deterioration encountered was in a man of 72 whose anergic invalidism was considered to be an independent but coincidental expression of his ageing.

(3) Certain Parkinsonian signs and symptoms could be observed to vary with the patient. Others appeared to be unaffected while for some no conclusions could be made.

Most subjective symptoms were lessened when the affective state was improved. The sense of effort was decreased, fatigue and anergia were less intense, and tiring was postponed. The patient was more indifferent to aching hypertonic muscles and was less restless. The discomfort of heat was tolerated better. An unresponsive limb was noticed less and did not seem so "weak" or "numb".

Parkinsonian tremor was lessened and motility increased and the patient was more active when he felt better. The tremor if mild in one limb might vanish and if severe it was reduced to less inconvenient proportions.

Certain conspicuous signs were not observed to vary with emotion. These were the rigidity, the poverty of movement, the specific postures and the facies of Parkinsonism.

There remained a group of physical signs which could not be studied because the psychological factors could not clearly be evaluated. These included the disorders of voluntary movement and effort such as muscular power, festination, slowness, stalling, clumsiness, and defects of gait, speech, writing, eating and swallowing. While the patient's activity was increased by psychotherapy the problem here was to distinguish, on the psychological side, the factor of voluntary and willing effort. It is this purposeful choosing and persisting which ultimately determines to what extent the residual motor system is mobilized and goes into action. How to measure voluntary effort was an unsolved dilemma.

No attempt was made to study autonomic and metabolic variations.

(4) The aggravating factors which could be treated were of some interest. The post-encephalitic group were usually younger people who had become accustomed to their handicap. In only four patients was there an important fear of becoming crippled. Their family responsibilities were usually less and their worries on this score were less. The younger cases of some years' duration were either single or were supported by a partner who had taken over the burden. Serious domestic discord was encountered in one patient. Their partners usually suffered more than they did in their marriages. On the other hand general management of the patient was of the greatest importance. Eighteen of them required more physical exercise, more occupation and more recreation.

The paralysis agitans group were older, of more recent and more rapid development. They commonly had heavy financial or family responsibilities which depended on a health they had expected to continue. It is not surprising that the troubles of this group were (1) fear of crippling and death in 8 patients, (2) family worry in 6 patients, and (3) fear of unemployment and poverty in 6 patients.

During this close observation certain conclusions were made regarding treatment: (1) The rigidity of Parkinsonism can be reduced by adequate doses of the standard preparations of stramonium, hyoscine and belladonna.

(2) The motor symptoms and tremor can be reduced and the patient will become more active if a state of confidence, fortitude and equanimity can be reached. Constitutional

factors can be stabilized by an environment which provides occupation, interest, recreation and activity as long as possible. Specific psychotherapy for acute reactive syndromes is essential. In most cases the need is for simple suggestion, encouragement, explanation, reassurance and re-education.

(3) Any clinical trial of the action of a drug on the Parkinsonian state requires an extensive and accurate study of the patient in his environment with his symptoms as well as his physical signs.

It is not without interest to reflect on the strategic advantage the family physician has in executing such a broad programme of treatment. Most of the patient's troubles could have been more conveniently managed by him than by the hospital clinic. Only the problems of doubtful diagnosis and severe neurosis and psychosis required the special experience of a consultant.

Contrecoup Lesions in the Relatively Severe Craniocerebral Injuries

By Major O. W. STEWART, R.C.A.M.C.

IN the past three years, 798 craniocerebral injuries have been admitted to the neurosurgical service of our hospital, excluding gunshot wounds. I would like to discuss briefly one group of contrecoup lesions that have been studied in this number.

The very nature of contrecoup lesions serves to emphasize the widespread extent of the injury.

In the following cases the contrecoup lesion in each instance was, to gross inspection, localized and moderately well demarcated; the presence of more diffuse but less severe injury could be deduced by clinical and, in some cases, pathological evidence. The reparative processes of these more extensive lesions may, however, be influenced by the more local lesion, if it continues to cause pressure on the surrounding brain or is responsible to a significant degree, for increased intracranial pressure. Such a condition materially affects the surgical rationale.

From a large number of post-mortem studies, Courville has deduced that when a projected head strikes on its side, the major contusion is a contrecoup one affecting the opposite temporal lobe. In these, adjacent portions of the frontal and parietal lobes may also be involved. When the blow is to the occipital region, contrecoup lesions of the frontal lobe is the rule. If the blow is to the left occipital region, the right frontal lobe suffers. Coup or direct lesions of the occipital lobes in such a case, in his opinion, are rare without a depressed fracture. When the blow is directed to the frontal region, Courville found direct contusions of the basilar surface of the frontal lobes but no instance of a contrecoup lesion of the occipital lobes.

From the study of our own cases—those with striking and localized cortical damage undeniably contrecoup in character—it seems most likely that the same mechanism must be responsible for some degree of damage in the majority of all closed head injuries. In some of the less severe ones, the generalized concussion or contusion is so slight that the signs and symptoms of the more localized contrecoup lesion may be manifested. Where there is severe generalized damage with marked disturbance of consciousness, the more delicate picture of the focal lesion is masked. Only in a certain group of these cases wherein the contrecoup lesion is relatively localized is surgical treatment of real value. In these, the history, clinical findings and chain of events show striking similarities.

Here are two examples of contrecoup frontal lesions:

The first case was a 29-year-old soldier, first seen in another hospital. He was slightly inebriated and about thirty minutes before admission had received a blow on the right occipital region. He *was conscious*, had walked in complaining of headache, was very restless but co-operative. He was transferred to our hospital seven days later when he was confused, restless, and incontinent. Motor, sensory and reflex examinations did not point to a localized brain contusion or compression. X-rays showed a linear fracture in the right occipital bone beneath the site of the blow. The pineal gland was well calcified and was displaced towards the right side a distance of 7 mm., and displaced downwards 1 cm. During an hour's observation, his condition deteriorated and he was explored. A small left subtemporal decompression was made and beneath the dura a solid subdural clot about 3/8 in. thick was found. This was sucked and syringed out. Frontal and posterior parietal burr holes were then made and at each site there was a thin subdural clot. It *was felt* at the time that no more should be done, although the size and amount of the clot did not seem sufficient to account for his condition. For the following twenty-four hours he remained drowsy but did not change greatly. On the second day following operation, his condition *deteriorated*, and he suddenly expired.

The post-mortem examination revealed a very large, solid, subdural hæmatoma surrounding the left frontal pole and beneath the left frontal lobe. There was clotted blood extruding from a laceration in the cortex and the brain adjacent to the hæmatoma and laceration was soft and friable. Had we been aware of the nature of this lesion, a frontal flap would have been turned down at the first and the entire lesion could have been dealt with. Such a procedure would undoubtedly have saved his life. His clinical course for the first seven days following the injury made it reasonable to assume that the amount of generalized brain injury was small in comparison with the local contre-coup injury.

We have now operated on 21 similar cases. In 4 the contrecoup lesion was in the frontal lobe following an occipital injury. The remainder involved the temporal lobes with adjacent frontal or parietal lobe injury in a few.

Here is another similar case:

A 20-year-old member of the W.A.A.F. was thrown from her bicycle, striking the right occipital region. She was unconscious for five or ten minutes but on admission to another hospital about forty-five minutes later was conscious but mildly confused and restless. There was a contusion of the right occipital scalp with a small superficial laceration in its centre. She was transferred to us three days later. Then, she was drowsy but easily roused. She complained bitterly of headache and her talk and reactions were somewhat facetious. In addition to the contusion and superficial laceration of the right occipital scalp there was some slight discoloration behind the right mastoid and blood behind the right tympanic membrane which had not ruptured. There was bilateral papilloedema. The only other abnormal neurological sign, apart from the facetiousness, was an extensor response to plantar stimulation on the right and diminished right abdo-minal reflexes. Lumbar puncture pressure was 350 mm. X-rays did not show a fracture but did show the pineal gland to be displaced slightly to the right of the mid-line and at the extreme posterior limits of the normal position. It was strongly suspected that she had a contrecoup laceration of the left frontal lobe with associated subdural clot and local oedema. However, inasmuch as her condition was fairly good, it was decided to wait and observe her further. During the next three days she seemed to improve slowly. She was less drowsy and was more coherent in her conversations. Despite this, her spinal fluid pressure remained elevated and the reflex changes persisted. During the evening of the sixth day following her injury, she complained more bitterly of headache, became very confused, getting in and out of bed and, for the first time, began voiding involuntarily. She was taken to the operating room and through a small left frontal bone flap the dura was found to be extremely tense with bluish discoloration beneath it. Almost the entire left frontal pole was softened and there was a fairly large solid clot over its surface and beneath it. The frontal pole was removed by irrigation and gentle suction, together with the clot. Following this the brain began to pulsate freely which it had not done before and the remaining portion of the hemisphere that was visible in the field became quite slack. Following operation she steadily improved with no evidence of elevated intracranial pressure clinically and this was supported by several lumbar punctures. The papilloedema subsided, the facetiousness disappeared and her discharge examination revealed no abnormal neurological findings. All tests failed to show any evidence of mental deterioration.

I will now describe two cases of contrecoup temporal lobe damage. The first of these was admitted a few hours following a motor-cycle accident. He was conscious though drowsy. Cranial nerves were normal except for a slight left peripheral facial palsy. All reflexes were normal. The X-rays showed a linear fracture involving the frontal, temporal and parietal bones entering the mastoid cells on the left. The pineal gland was calcified and shifted 2·5 mm. to the left of the mid-line (towards the fracture). In the absence of any abnormal neurological signs and considering his state of conscious-ness, it was felt that he should be observed further, despite the fact that the pineal gland was displaced. Œdema of the hemisphere alone may and does displace the pineal. He was re-examined frequently for any change, bearing in mind the likelihood of a contrecoup lesion. The mental state improved and all signs remained unchanged until seven days after the injury when he became drowsy and complained bitterly of right frontal head-ache. Then, his pupils were equal, the retinal veins were full, the left ankle-jerk was increased over the right, the left abdominal and cremasteric reflexes were diminished. Plantar stimulation on the left gave an extensor response, on the right—a flexor response. Cerebrospinal fluid pressure was 290 mm.

Operation revealed a laceration of the temporal lobe with some localized softening and a large subdural clot covering the temporal pole and the middle fossa beneath the temporal lobe. This patient has made an excellent recovery.

A second case presented the typical contrecoup temporal lobe lesion but was associated with considerable direct trauma to the brain on the side of injury due to a depressed fracture and the total injury was extensive. He was admitted soon after a motor-cycle accident. There was a comminuted and depressed fracture of the right parietal bone. The pineal gland was not seen. He was semiconscious with spasticity of all four extremities.

At operation extensive damage to the right parietal cortex was found. The fragments were elevated and a large decompression left. He gradually improved for the next ten days. The decompression then began to bulge and he became much drowsier with new objective signs which pointed to a lesion of the left cortex. A small needle was passed into the right lateral ventricle through a small stab wound in the scalp at

the upper margin of the bone defect. 30 c.c. of fluid under pressure were withdrawn and 20 c.c. of oxygen injected. X-rays following this procedure showed a marked shift of the ventricles toward the side of fracturing and initial operation (right).

The left side was explored and the typical lesion found and removed. His pressure from then on remained normal and he slowly improved but was left with very severe cerebral impairment which was known to be present from the outset.

Summary and Conclusions

In this discussion the possibility of contrecoup damage in closed head injuries is emphasized.

The consistency in relationship between the site of the blow and the site of maximum cerebral damage has been borne out by post-mortem and clinical observations with occasional individual variants.

It is therefore important to determine, whenever possible, the point of impact on the skull. If local scalp lesions or a definite history do not give this information, the fracture line, when present, gives a rough location. In the majority of cases objective signs of focal damage are not evident.

The cases described are typical of a *small* group out of the total number of closed craniocerebral injuries. In our series—22 out of 798 present similar problems in gross pathology, diagnosis and treatment. In them the predominantly localized lesion of either the temporal or frontal lobe, after a period of from five to ten days, begins to act as a rapidly expanding space-occupying lesion by exerting local pressure on the brain adjacent to it and causing generalized increased intracranial pressure. This is *not* due to continued hæmorrhage.

The diagnosis depends first on an awareness of this type of lesion and the mechanism by which it is produced, with careful and repeated clinical examinations. Ofttimes the first sign will be a change in the level of consciousness, which in several of our cases was recognized initially by the Sister. This alteration in the patient's course usually occurs between the fifth and tenth day after the injury.

The X-rays are valuable in demonstrating a fracture line and displacement of the pineal gland when that structure is sufficiently calcified to be visible. Occasionally it may be desirable to visualize the ventricles with oxygen.

The surgical treatment is removal of the damaged area lesion, thereby giving an internal decompression as well. This removal of destroyed brain tissue and blood clot relieves immediately the pressure on the viable but injured adjacent cortex and reduces the generally increased intracranial pressure, which, with its vicious side effects, is the arch-enemy of brain healing.

[*February* 3, 1944]

Venous Thrombosis in the Central Nervous System

By J. Purdon Martin, M.D.

Venous thrombosis affecting the central nervous system is evidently very much less common than it used to be. MacEwan in his classical work on pyogenic diseases of the brain written fifty years ago stated that venous thrombosis was *more common* within the cranium than in any other place in the body. Two groups of cases were recognized —"marantic" (or wasting) and infective; Gowers, who knew everything in clinical neurology, recognized also a group occurring in the puerperal state.

Septic sinus thrombosis is much more widely known than aseptic. In the septic type of case the clinical picture is composed of three or four groups of symptoms: Those due to the infective state, those due to obstruction of the sinus involved and those resulting from veins draining into it, and perhaps also local signs at the site of the original infection. In the aseptic case, however, we have a better opportunity of recognizing the effects of thrombosis of sinuses and veins in their purity.

The picture which results is often compounded of the signs and symptoms due to the obstruction of a sinus and those due to thrombosis of veins draining into it. However these groups are not necessarily combined. Sinuses may thrombose without thrombosis occurring in their entering veins, and veins may thrombose without the occurrence of sinus thrombosis or obstruction.

The post-mortem examination revealed a very large, solid, subdural hæmatoma surrounding the left frontal pole and beneath the left frontal lobe. There was clotted blood extruding from a laceration in the cortex and the brain adjacent to the hæmatoma and laceration was soft and friable. Had we been aware of the nature of this lesion, a frontal flap would have been turned down at the first and the entire lesion could have been dealt with. Such a procedure would undoubtedly have saved his life. His clinical course for the first seven days following the injury made it reasonable to assume that the amount of generalized brain injury was small in comparison with the local contre-coup injury.

We have now operated on 21 similar cases. In 4 the contrecoup lesion was in the frontal lobe following an occipital injury. The remainder involved the temporal lobes with adjacent frontal or parietal lobe injury in a few.

Here is another similar case:

A 20-year-old member of the W.A.A.F. was thrown from her bicycle, striking the right occipital region. She was unconscious for five or ten minutes but on admission to another hospital about forty-five minutes later was conscious but mildly confused and restless. There was a contusion of the right occipital scalp with a small superficial laceration in its centre. She was transferred to us three days later. Then, she was drowsy but easily roused. She complained bitterly of headache and her talk and reactions were somewhat facetious. In addition to the contusion and superficial laceration of the right occipital scalp there was some slight discoloration behind the right mastoid and blood behind the right tympanic membrane which had not ruptured. There was bilateral papillœdema. The only other abnormal neurological sign, apart from the facetiousness, was an extensor response to plantar stimulation on the right and diminished right abdo-minal reflexes. Lumbar puncture pressure was 350 mm. X-rays did not show a fracture but did show the pineal gland to be displaced slightly to the right of the mid-line and at the extreme posterior limits of the normal position. It was strongly suspected that she had a contrecoup laceration of the left frontal lobe with associated subdural clot and local œdema. However, inasmuch as her condition was fairly good, it was decided to wait and observe her further. During the next three days she seemed to improve slowly. She was less drowsy and was more coherent in her conversations. Despite this, her spinal fluid pressure remained elevated and the reflex changes persisted. During the evening of the sixth day following her injury, she complained more bitterly of headache, became very confused, getting in and out of bed and, for the first time, began voiding involuntarily. She was taken to the operating room and through a small left frontal bone flap the dura was found to be extremely tense with bluish discoloration beneath it. Almost the entire left frontal pole was softened and there was a fairly large solid clot over its surface and beneath it. The frontal pole was removed by irrigation and gentle suction, together with the clot. Following this the brain began to pulsate freely which it had not done before and the remaining portion of the hemisphere that was visible in the field became quite slack. Following operation she steadily improved with no evidence of elevated intracranial pressure clinically and this was supported by several lumbar punctures. The papillœdema subsided, the facetiousness disappeared and her discharge examination revealed no abnormal neurological findings. All tests failed to show any evidence of mental deterioration.

I will now describe two cases of contrecoup temporal lobe damage. The first of these was admitted a few hours following a motor-cycle accident. He was conscious though drowsy. Cranial nerves were normal except for a slight left peripheral facial palsy. All reflexes were normal. The X-rays showed a linear fracture involving the frontal, temporal and parietal bones entering the mastoid cells on the left. The pineal gland was calcified and shifted 2·5 mm. to the left of the mid-line (towards the fracture). In the absence of any abnormal neurological signs and considering his state of conscious-ness, it was felt that he should be observed further, despite the fact that the pineal gland was displaced. Œdema of the hemisphere alone may and does displace the pineal. He was re-examined frequently for any change, bearing in mind the likelihood of a contrecoup lesion. The mental state improved and all signs remained unchanged until seven days after the injury when he became drowsy and complained bitterly of right frontal head-ache. Then, his pupils were equal, the retinal veins were full, the left ankle-jerk was increased over the right, the left abdominal and cremasteric reflexes were diminished. Plantar stimulation on the left gave an extensor response, on the right—a flexor response. Cerebrospinal fluid pressure was 290 mm.

Operation revealed a laceration of the temporal lobe with some localized softening and a large subdural clot covering the temporal pole and the middle fossa beneath the temporal lobe. This patient has made an excellent recovery.

A second case presented the typical contrecoup temporal lobe lesion but was associated with considerable direct trauma to the brain on the side of injury due to a depressed fracture and the total injury was extensive. He was admitted soon after a motor-cycle accident. There was a comminuted and depressed fracture of the right parietal bone. The pineal gland was not seen. He was semiconscious with spasticity of all four extremities.

At operation extensive damage to the right parietal cortex was found. The fragments were elevated and a large decompression left. He gradually improved for the next ten days. The decompression then began to bulge and he became much drowsier with new objective signs which pointed to a lesion of the left cortex. A small needle was passed into the right lateral ventricle through a small stab wound in the scalp at

of the damage in the cerebral tissue. The hemiplegia may be complete or partial; its greater incidence may be on the arm or on the leg; speech is rarely involved, but I have seen one instance of complete right hemiplegia with total aphasia. When veins on both sides of the longitudinal sinus are affected there may be a particular degree of spasticity and weakness in the lower limbs, as Holmes and Sargent described, and I have even seen subconvulsive spasms of extensor rigidity going on in the limbs of a comatose patient; but when thrombosis is unilateral the upper limb is usually the more affected. The *visual symptoms* that result from thrombosis of the more posterior veins in the superior surface of the brain are very interesting. The last of the veins ascending to the sagittal sinus lies in the parieto-occipital fissure and the angular gyrus is part of its territory. On two occasions I have seen word-blindness as part of the symptomatology and in two other instances visual disorientation. This latter symptom if complete indicates that both sides of the brain must be involved, because each angular gyrus is concerned only with one half field. Complete visual disorientation, therefore, indicates that thrombosis has occurred on both sides of the cerebrum, and so provides a strong presumption that clot is present in the sagittal sinus. In one of my cases the patient recovered the function on one side and was then unconscious of any disability.

Prognosis.—The immediate prognosis is difficult. In the convulsive stage the symptoms are always very alarming, but fatalities are few. Once the convulsive stage is over recovery from the hemiplegia may be rapid, and may be more or less complete in a fortnight. Exaggerated tendon-jerks, extensor plantar reflexes and some stiffness of the proximal parts of an affected limb may remain. There are, however, many cases in which recovery is very imperfect and, in fact, the most complete and most spastic hemiplegia may be left as a permanent disability. The visual symptoms present the same variability of outlook. In general it can be said that the prognosis for the recovery of function is much better than in cases of arterial thrombosis, and is, in a large proportion of cases, good. *Petit mal* may occur as a sequel and further thrombosis may take place even after many months.

CASES ASSOCIATED WITH CHILDBIRTH

In most of the cases associated with childbirth the manifestations of thrombosis in cranial sinuses or cerebral veins develop during the puerperium and generally between four and twenty-one days after confinement. I have encountered two cases and a probable third in which the symptoms developed during pregnancy (two of these were the cases with visual disorientation), and in each instance the patient had a stillborn child, pointing to the possibility that thrombosis may have occurred first in the placenta. The reason why thrombosis, associated with childbirth, occurs within the cranium may be because of "metastases". In the vertebral canal, and winding in and out between the laminæ, there is a large plexus of veins. Little attention has been paid to this plexus in the recent teaching of anatomy, but about one hundred years ago it was evidently prominent in the minds of anatomists. Bock described it in 1824; Breschet gave a new description of it in 1837; Bonamy illustrates it in "Traité d'Anatomie", (Second Edition, published in 1844); Cruveilhier a little later gave another very good description. According to Professor H. A. Harris a clear account of these veins was given by Samuel Willis in 1664 and another by Winslow in 1732. In the post-mortem room, the main vessels of this plexus are easily seen in the lower half of the vertebral canal after removal of the theca; they lie lateral to the ligamentous tissue which lines the anterior wall of the canal. In recent times Batson has injected these veins with radio-opaque material and has shown that the material passes up from the veins on the floor of the pelvis to the cranial sinuses. There is no doubt that the passage is free as far as the base of the cranium, and it is continued into the cranium by quite a number of veins of smaller size; the great occipital vein, connecting the lateral sinus; the mastoid vein similarly; other veins passing in on the back and front of the foramen magnum to enter the occipital sinuses and the basilar sinus respectively; others, again, entering through the hypoglossal and other foramina to form similar connexions. The possibility then exists that some element may pass up by this route from the pelvis or from the lower limbs to the cranial sinuses. If something does pass up it seems most likely it is a small piece of clot, because we know that such pieces of clot are dislodged from the pelvis; they may find their way into the iliac veins, and so cause pulmonary emboli; but pieces of meconium and other elements derived from the amniotic fluid are also said to find their way into the circulation. There are two special factors that may be responsible for *directing a fragment of clot occasionally into the vertebral veins.* The first is pressure on the vena cava, or on the iliac veins, and the second is the great enlargement of the pelvic vessels during *pregnancy,* in which the veins on the floor of the pelvis connecting with the vertebral veins and

A sinus is in the nature of a channel receiving many veins, and is anatomically separated from the brain. In general, thrombosis of a sinus without thrombosis of associated veins on the brain produces widespread, or general, obstructive effects such as œdema or intracranial pressure. Such cases are by no means uncommon and result from ear disease or from enteritis. Among the unusual causes of sinus thrombosis that I have encountered I must mention head injuries. Holmes and Sargent described cases resulting from bullet wounds grazing the skull, but I have seen two cases due to closed head injuries, and when after such an injury the intracranial pressure becomes greatly raised, the possibility of sinus thrombosis should therefore be kept in mind. A peculiar cause of thrombosis in the cavernous sinuses which I have met with twice is the rupture of (or leakage from) an aneurysm of the carotid artery within the sinus. In each of these cases the patient became blind within a few days. The first patient recovered his sight and is said to have left hospital without any disability. The other remained completely blind; she died after a few weeks from bronchopneumonia, and the diagnosis was confirmed post mortem. The optic nerves showed gross degenerative charges.

In contrast to the sinuses the cerebral veins come into intimate relationship with the brain and notwithstanding the free anastomosis between them and the presence of alternative channels for the blood flow, thrombosis often produces surprisingly severe effects. Thrombosis of cerebral veins in the complete absence of clot in their related sinus is admittedly not common. I see, however, little reason to separate such cases from those in which the vein is obstructed by a small mural clot at its entrance into the superior longitudinal sinus and this appears to be a common site of the first thrombus. An American paper says that the first case of cerebral venous thrombosis was described by Dowman in 1926, but in the *British Medical Journal* of 1888, p. 1011, there is the record of one described by Scougal, and Money briefly described one in a child in 1890. Dowman's may have been the first recorded case in which the condition was seen at operation. The Rolandic vein was very large and bluish black: it was hard to the touch and could be rolled under the fingers. The patient made a complete recovery. Also, in a case described by Davis in 1933, thrombosed veins were revealed by an exploratory craniotomy. The most striking features were the intensely blue and distended veins, which felt hard to the touch. The Rolandic vein was as large and as hard as a slate pencil, while the cortex over which it lay was grey instead of the usual pink. After exploration with a hypodermic needle the vein was opened for a length of 1 cm., and a dark brown clot was found; an attempt was made to suck it out, but without much success. The patient died two days later. The thrombus in the Rolandic vein was 3 cm. in length, and its upper end was evidently about 2 cm. from the junction of the vein with the superior longitudinal sinus.

The physical effects of venous thrombosis of the brain can best be appreciated by recalling the arresting picture presented by venous thrombosis in the retina. The vein is distended with dark or possibly red clot; the small tributary veins rupture, with greater or less extravasation of blood, and, what is more important, with immediate loss of function, and eventual degeneration of tissue in the territory drained by the affected vessel. Similar effects occur in the brain.

The degree of these changes depends, not only on the size of the vein affected, but also on the abruptness with which thrombosis extends and the circulation becomes impaired. Thus it may be that preceding obstruction of the sinus into which the vein drains may cause a preliminary opening-up of alternative drainage and so actually mitigate the effects of thrombosis spreading into the vein secondarily.

Clinical signs depend on the areas affected. Abrupt thrombosis of the motor area often gives rise to severe convulsive phenomena. These are often of dramatic severity and fulminating in their onset. The convulsion is likely to begin with a local sign and rapidly become generalized, and when the convulsions are over the patient is left hemiplegic. On the other hand, the onset may be much less dramatic, and the patient may become hemiplegic without any convulsion or unconsciousness, and with little, or no manifestation of shock. Why convulsions occur in some cases and not in others, we have not yet determined. Convulsions have seemed to me to be less frequent when there were signs of obstruction of the longitudinal sinus. Whether there is any correlation between convulsions and extravasation of blood we do not know. And again, convulsions may be associated with less severe destruction of nervous elements in the first instance. If the thrombosis is situated at a distance from the motor area the symptoms often appear without convulsive phenomena, e.g. with lesions in the pre-frontal area convulsions are not common, although some degree of weakness may develop, and when the lesions are posterior to the central gyri convulsions, in my experience, do not occur.

The other clinical features depend more precisely on the degree and site and extent

Dr. Dorothy Russell kindly examined sections. In the superior longitudinal sinus the lining endothelium was in places impregnated with a thick mat of fibrin. This was more conspicuous in the posterior portion than the anterior: in the latter one short segment of the endothelium alone showed this change. In the posterior part there were in addition occasional tongues of fibrin covering the surface of the endothelium in side channels of the main sinus bordered by arachnoid villi. No fibrin, however, was found on the actual surfaces of the villi. The findings in this case therefore suggested that the cause of the increased intracranial pressure was obstruction of venous outflow, not impediment of absorption of the cerebrospinal fluid. What then can be the explanation of the cases in which jugular compression causes an equal and normal rise on both sides? Barnes Woodhall (1936) has made anatomical studies as the result of which he questions the validity of Queckenstedt's test as evidence of lateral sinus obstruction, suggesting that in some cases the collateral circulation is so free that pressure set up by jugular compression may by-pass the obstruction. Yet if this be so one might expect the collateral circulation to work equally in the reverse direction preventing intracranial venous engorgement. It may be that the observation here recorded of clot extending from one lateral sinus far enough into the superior longitudinal sinus to obstruct the entrance of the other was a clue to the mechanism of increased intracranial pressure in those cases. More direct evidence should be obtained by X-ray using the method of injecting contrast media into the superior longitudinal sinus described by Frenckner (1937).

The cranial nerve palsies associated with intracranial thrombophlebitis are of some interest. In the otitic cases with increased intracranial pressure the frequency of 6th nerve involvement—usually on the side of the affected ear, and therefore presumably on the side of the affected lateral sinus—is striking and suggests the possibility of a direct involvement of this nerve through the inferior petrosal sinus. If this be the correct explanation it might also hold for Gradenigo's syndrome and might explain why the 6th nerve palsy in a number of these cases develops from an acute otitis media with little or no pain or constitutional disturbance, and recovers without operative interference, the supposition in these cases being that there is an aseptic thrombosis of the sinus with extension of the inflammatory process through its wall to the nerve which lies adjacent to it in Dorello's canal. Much more rarely paralysis of the 9th, 10th and 11th nerves may be observed in association with otitis media, or with thrombophlebitis originating either in the lateral or the cavernous sinus.

In a paper dealing with cranial nerve palsies in otitis media I (Symonds, 1927) recorded four cases of this kind. One was that of a girl, aged 6, who after an acute left otitis media developed a left 6th nerve palsy at a time when her ear was discharging freely and her general condition was good. Shortly afterwards she had paralysis of soft palate, sternomastoid and trapezius on the same side. The mastoid was subsequently drained and complete recovery ensued. This case reviewed in the light of present speculation suggests thrombosis of inferior petrosal sinus by direct spread from the ear with first forward, and then backward extension. Involvement of the 9th, 10th and 11th nerves has also been observed after lateral sinus thrombosis from tonsillar infection. I have recently seen a case of cavernous sinus thrombosis of the type which would almost certainly have been fatal before the introduction of sulfa drugs in which the symptoms suggested an extensive spread into communicating venous channels. The origin of the infection was a cellulitis and the early signs those of a cavernous sinus thrombosis with much proptosis and chemosis of the left eye, papilloedema and paralysis of all ocular movements, and comparable but incomplete signs on the right. After a critical period of septicæmia treated with sulphanilamide he recovered but developed paræsthesiæ on the right side of the face with complete paralysis of the 5th motor root. This recovered in the course of a week or two and paralysis of the right soft palate was then observed with loss of sensation in the glossopharyngeal distribution. Later he developed severe headaches with a raised cerebrospinal fluid pressure and epileptic attacks beginning with adversion to the left and becoming generalized. The story suggests extension of thrombophlebitis backwards on the right along superior and inferior petrosal sinuses, and also to the cortical veins and possibly the superior longitudinal sinus. It seems likely that chemotherapeutic success in septicæmia may provide more opportunities of observing and classifying the clinical signs of intracranial thrombophlebitis than has previously been possible.

REFERENCES

FRENCKNER, P. (1937) *J. Laryng.*, **52**, 350.
GARDNER, W. J. (1939) *Arch. Otolaryng.*, **30**, 253.
SYMONDS, C. P. (1927) *J. Laryng.*, **42**, 656.
WOODHALL, BARNES (1936) *Arch. Surg.*, London, **33**, 297.

some of the vertebral veins themselves probably share. If any element does pass up it leaves, as a rule, no trace of its passage. One of my patients, however, developed complete paraplegia two days after a septic abortion, and post mortem there was an abscess surrounding and involving the theca at the 9th dorsal vertebra and no abscess anywhere else in the body. In another case of septic abortion the only abscess was in the brain. Both of these cases suggest that septic material had passed up from the pelvis to the spinal cord and to the brain by a route which did not involve the general circulation. It seems to me probable that this route was by way of the vertebral veins, and that in non-septic cases some element of clot passes up to the cranium by the same channel.

Finally, there is the possibility of venous lesions affecting the spinal cord. I have already mentioned that one of my puerperal patients with sinus thrombosis had also a spinal lesion, and probably that lesion too was venous and thrombotic. In another case of venous thrombosis, not puerperal, the patient also had a spinal lesion (from which she made a very good recovery). It is likely that isolated lesions of the spinal cord associated with mild infectious conditions, such as boils, may be due to venous thrombosis.

<div align="center">REFERENCES</div>

DOWMAN, C. E. (1926) *Arch. Neur. & Psych.*, **15**, 110.
DAVIS, D. B. (1933) *J. Nerv. & Ment. Dis.*, **77**, 22.

Dr. C. P. Symonds : It is interesting to look back into the records of cases of obscure hemiplegia and find that in some of them the diagnosis of cerebral thrombophlebitis offered the solution. Turning to the cases with increased intracranial pressure clinical observation has shown that papilloedema with a high cerebrospinal fluid pressure and an air picture of normal ventricles may follow thrombosis of the dural sinuses beginning in the lateral sinus usually from otitis, but sometimes from tonsillitis or other source of local infection; or in the superior longitudinal sinus from frontal sinusitis; or in the cavernous sinus. The same clinical picture may sometimes be seen in puerperal thrombophlebitis where there is no clue to the point of origin of the intracranial thrombosis.

The otitic cases are the commonest and have been most thoroughly studied. The story in those cases is usually that of lateral sinus thrombosis. The simplest explanation of increased intracranial pressure from lateral sinus thrombosis is venous engorgement resulting from obstruction of the outflow, but clinical observation in some cases fails to support this assumption. I have published examples in which the rise of cerebrospinal fluid on jugular compression was normal on both sides, and others have since been recorded. In Gardner's (1939) series of 10 cases described as otitic sinus thrombosis causing intracranial hypertension there were two in which jugular compression showed no evidence of lateral sinus obstruction, and a third in which this test was not performed but at operation, though a peri-sinus abscess was found, the lateral sinus was patent. Because of such evidence and because the same picture of increased intracranial pressure may be observed following frontal sinusitis, with visible proof of thrombosis in the anterior part of the superior longitudinal sinus, it may be that the common factor in all those cases is not obstruction to the venous outflow from the skull but impediment to the absorption of cerebrospinal fluid through the arachnoid villi. In order to produce this effect the superior longitudinal sinus need not necessarily be obstructed: mural thrombophlebitis without obstruction might be sufficient. A specimen which I obtained in August 1939 through the kindness of Mr. R. J. Cann of Guy's Hospital offered the chance of testing this hypothesis. A woman, aged 20, was admitted to hospital with a history of acute right earache three weeks previously. A week later she began to have severe generalized headaches. A week after this the right ear discharged, the earache diminished but the headache continued and she became increasingly drowsy. On admission she could just be roused: there was bilateral papilloedema with no localizing signs. The right auditory meatus contained pus. Lumbar puncture gave a clear fluid with a pressure of 350 mm., containing no cells and sterile on culture. Owing to some doubt as to the pressure reading a second lumbar puncture was done four hours after the first, with a similar reading. This was 5 p.m. At 6 a.m. next morning the Sister spoke to her and noticed no material change in her condition. Five minutes later she was found dead. At post-mortem the right lateral sinus contained ante-mortem clot as far as its junction with the superior longitudinal sinus. The left lateral sinus was normal and the smaller of the two. The superior longitudinal sinus was opened in its whole length and no gross changes found. On following this down to its posterior end the clot in the right lateral sinus became visible before the straight sinus or the left lateral sinus was opened, so that it appeared that the clot, originating in the right lateral sinus, was obstructing both lateral sinuses.

Dr. Dorothy Russell kindly examined sections. In the superior longitudinal sinus the lining endothelium was in places impregnated with a thick mat of fibrin. This was more conspicuous in the posterior portion than the anterior: in the latter one short segment of the endothelium alone showed this change. In the posterior part there were in addition occasional tongues of fibrin covering the surface of the endothelium in side channels of the main sinus bordered by arachnoid villi. No fibrin, however, was found on the actual surfaces of the villi. The findings in this case therefore suggested that the cause of the increased intracranial pressure was obstruction of venous outflow, not impediment of absorption of the cerebrospinal fluid. What then can be the explanation of the cases in which jugular compression causes an equal and normal rise on both sides? Barnes Woodhall (1936) has made anatomical studies as the result of which he questions the validity of Queckenstedt's test as evidence of lateral sinus obstruction, suggesting that in some cases the collateral circulation is so free that pressure set up by jugular compression may by-pass the obstruction. Yet if this be so one might expect the collateral circulation to work equally in the reverse direction preventing intracranial venous engorgement. It may be that the observation here recorded of clot extending from one lateral sinus far enough into the superior longitudinal sinus to obstruct the entrance of the other was a clue to the mechanism of increased intracranial pressure in those cases. More direct evidence should be obtained by X-ray using the method of injecting contrast media into the superior longitudinal sinus described by Frenckner (1937).

The cranial nerve palsies associated with intracranial thrombophlebitis are of some interest. In the otitic cases with increased intracranial pressure the frequency of 6th nerve involvement—usually on the side of the affected ear, and therefore presumably on the side of the affected lateral sinus—is striking and suggests the possibility of a direct involvement of this nerve through the inferior petrosal sinus. If this be the correct explanation it might also hold for Gradenigo's syndrome and might explain why the 6th nerve palsy in a number of these cases develops from an acute otitis media with little or no pain or constitutional disturbance, and recovers without operative interference, the supposition in these cases being that there is an aseptic thrombosis of the sinus with extension of the inflammatory process through its wall to the nerve which lies adjacent to it in Dorello's canal. Much more rarely paralysis of the 9th, 10th and 11th nerves may be observed in association with otitis media, or with thrombophlebitis originating either in the lateral or the cavernous sinus.

In a paper dealing with cranial nerve palsies in otitis media I (Symonds, 1927) recorded four cases of this kind. One was that of a girl, aged 6, who after an acute left otitis media developed a left 6th nerve palsy at a time when her ear was discharging freely and her general condition was good. Shortly afterwards she had paralysis of soft palate, sternomastoid and trapezius on the same side. The mastoid was subsequently drained and complete recovery ensued. This case reviewed in the light of present speculation suggests thrombosis of inferior petrosal sinus by direct spread from the ear with first forward, and then backward extension. Involvement of the 9th, 10th and 11th nerves has also been observed after lateral sinus thrombosis from tonsillar infection. I have recently seen a case of cavernous sinus thrombosis of the type which would almost certainly have been fatal before the introduction of sulfa drugs in which the symptoms suggested an extensive spread into communicating venous channels. The origin of the infection was a cellulitis and the early signs those of a cavernous sinus thrombosis with much proptosis and chemosis of the left eye, papilloedema and paralysis of all ocular movements, and comparable but incomplete signs on the right. After a critical period of septicæmia treated with sulphanilamide he recovered but developed paræsthesiæ on the right side of the face with complete paralysis of the 5th motor root. This recovered in the course of a week or two and paralysis of the right soft palate was then observed with loss of sensation in the glossopharyngeal distribution. Later he developed severe headaches with a raised cerebrospinal fluid pressure and epileptic attacks beginning with adversion to the left and becoming generalized. The story suggests extension of thrombophlebitis backwards on the right along superior and inferior petrosal sinuses, and also to the cortical veins and possibly the superior longitudinal sinus. It seems likely that chemotherapeutic success in septicæmia may provide more opportunities of observing and classifying the clinical signs of intracranial thrombophlebitis than has previously been possible.

REFERENCES

FRENCKNER, P. (1937) *J. Laryng.*, **52**, 350.
GARDNER, W. J. (1939) *Arch. Otolaryng.*, **30**, 253.
SYMONDS, C. P. (1927) *J. Laryng.*, **42**, 656.
WOODHALL, BARNES (1936) *Arch. Surg., London*, **33**, 297.

Miss Diana Kinloch Beck: In the experimental work to be described, Dr. Dorothy Russell and I have aimed at establishing, by some means, a spreading thrombophlebitis originating in the superior longitudinal sinus.

Despite certain authoritative statements to the contrary the experimental production of thrombosis in the peripheral veins has been shown to be quite a difficult problem but it might be supposed, from a consideration of certain well-known anatomical and physiological peculiarities of the superior longitudinal sinus and its tributary veins, that efforts to produce thrombosis therein would be comparatively easy.

So far as we are aware, only one attempt has been made in this direction. In one dog, Bize (1931) occluded the torcular Herophili and hind end of the superior longitudinal sinus with a tampon of iodoform gauze, and in a second dog he injected 1 c.c. of quinine urethane solution at the same site; in neither experiment was there any significant consecutive clinical or pathological change.

We have attempted by the following measures to induce thrombosis in the longitudinal sinus in rabbits, cats and dogs with remarkable lack of success.

(1) *Inducement of stasis* in the rabbit by occlusion of the lumen at one (four experiments) or two points (three experiments). No thrombosis was found after survival for periods varying from two days to three weeks. We did not anticipate that this would be effective but considered that any possible effects of occlusion should be gauged before proceeding further.

(2) Combination of this procedure in the rabbit with *the injection of coagulants* into the lumen: (a) A physiological coagulant: thrombin (five experiments); (b) a chemical coagulant: ethamolin (nine experiments).

In practice up to 0·1 c.c. of the coagulant was slowly injected into a segment of the sinus, occluded at either end for a period of two minutes. The dilutions of the thrombin used, though effecting coagulation *in vitro*, produced no effect *in vivo*. The ethamolin though not the thrombin, invariably produced thrombosis, in precisely similar circumstances in the marginal vein of the rabbit's ear, but failed to act similarly in the superior longitudinal sinus.

Repetition of the ethamolin injections in the dog (three experiments) similarly failed in their object.

(3) *Heat coagulation* (two experiments).—In two dogs the dorsal well of the sinus was cauterized down to the intima over segments measuring 0·4 and 1·5 cm. respectively. Examination after four and six days showed no thrombosis beyond minute fragments in the adjacent lacunæ.

(4) *Mechanical blockage of the lumen* in dogs.—(a) *By muscle*: A portion of the temporal muscle, beaten into a small "stamp" was introduced (two experiments) through a small opening in the dorsal wall of the sinus by traction on an attached thread. The hæmorrhage incidental to this manœuvre was immediately arrested on the entry of the muscle into the lumen. Although such muscle stamps are powerful hæmostatic agents in neurosurgical operations, they failed to effect thrombosis in these experiments. We therefore, in a further series of four dogs, steeped the muscle in ethamolin for twenty to thirty minutes before inserting it into the sinus in order to injure the endothelium. No difference in effect was obtained. The muscle underwent organization and recanalization in the course of three months.

(b) *By cotton-wool soaked in ethamolin* (three experiments): It was considered that blockage by a foreign substance, such as cotton-wool, might effectively occlude the sinus for a longer period.

In two of our animals slight dilatation of a lateral ventricle was found to coincide with a maximal blockage of the sinus (2·5 cm.). Though this asymmetrical dilatation was not impressive we felt it would be worth while to block an even greater length.

(5) For this we selected very young animals in view of the high incidence of sinus thrombosis in young subjects. A further advantage lay in the circumstance that the sutures in these animals were still open.

We succeeded in getting litters of young puppies and kittens aged 6 to 8 weeks. By using two elongated pledgets of ethamolinized cotton-wool, and passing these both fore and aft from a central point of entry on the fully exposed sinus we succeeded in obliterating lengths varying from 1/2 to 5/6 of the whole longitudinal sinus.

TABLE.

PUPPIES		KITTENS	
Aged 6 to 7 weeks		Aged 6 to 8 weeks	
Survival 5 to 10 weeks		Survival 5 to 7 weeks	
(1 died 36 hours after operation)			
Length S.L.S.	Proportion occluded	Length S.L.S.	Proportion occluded
4·2 cm.	5/6	4·3 cm.	4/7
5·5 cm.	2/3	3·8 cm.	1/2
6·0 cm.	2/3	3·7 cm.	2/3
5·8 cm.	7/12	4·2 cm.	5/7

Transverse section of the sinus in all instances showed complete blocking of the lumen throughout the operation area; in time the cotton-wool fibres were subjected to the activity of macrophages and the area became organized by fibrous tissue containing blood-vessels.

In animals in which a maximal length of the sinus was occluded there developed fullness of the veins of the fundus but there was no loss of definition of the disc edges. All our animals maintained perfect health up to the time of being killed, with the exception of one puppy which died thirty-six hours after operation, apparently from loss of blood.

In no experiment was there either thrombosis of the adjacent lumen in front of or behind the site of blockage, or of any of the superficial cerebral veins. No ventricular dilatation appeared in any of the kittens. A variable but slight dilatation was found in the puppies. This difference may be explained by the paucity of venous tributaries to the superior longitudinal sinus in the kitten. Though these are more numerous in the dog, they are fewer than in man.

DISCUSSION

We are forced to conclude that, at any rate in the dog and cat, the greater part of the superior longitudinal sinus can be suddenly obliterated without any gross inconvenience to the animal. Evidently the collateral circulation is so good that it can at once compensate for such a disturbance. It should be noted that the anastomoses between cerebral and diploic veins, demonstrated by Cushing to be abundant and of great importance in the dog, were necessarily sacrificed in the operative exposure of the sinus wall.

It is possible that a condition analogous to that of "otitic hydrocephalus" in man can only be produced experimentally by inducing a thrombosis that will spread from the main sinus into the adjacent lacunæ and the mouths of the venous tributaries.

Reviewing the published reports of human cases of this kind one is struck by the frequency with which an infective process is present in some part of the body although the thrombosis of the intracranial sinuses is essentially aseptic. It may be—and the idea is not new—that tissue-immunity is a factor deserving of more attention in this connexion. With this in mind we have recently been attempting to reproduce the Shwartzmann phenomenon in the walls of the superior longitudinal sinus in rabbits.

The mechanism of this reaction is unknown: in practice a sensitizing dose of a sterile filtrate prepared from a bacterial culture is delivered either into the skin, or in our attempts, to the scarified wall of the sinus. Within twenty-four hours a so-called precipitating dose of the same filtrate is injected intravenously. A positive reaction is shown by hæmorrhages and necrosis of the tissues at the site of sensitization. Up to date we have tried this in three rabbits only and have obtained necrosis and an inflammatory reaction in the pericranium and other soft tissues external to the dura. We await histological examination before reporting any reaction in the sinus wall.

(This work when completed will be reported fully elsewhere.)

Reference.—BIZE, P. R. (1931) L'hydrocephalie ventriculaire. Paris.

Major John E. Scarff, U.S.A.M.C.: In 1933, while exploring the exposed cortex of a human subject on the operating table with an electric current, in search of an epileptogenic focus in a case of focal epilepsy, it was observed that the trigger zone was immediately adjacent to a large pacchionian granulation. On the assumption that this might be acting as an adhesion, the pacchionian granulation was divided thus freeing the vein at this point from its attachment to the superior longitudinal sinus. In doing this all of the communicating veins passing over the cortex to the sinus through the pacchionian granulation were necessarily ligated and divided. The improvement in the patient's epilepsy which followed this procedure warranted its repetition in other cases.

Between 1933 and 1942 one or more pacchionian granulations with their attendant vein had been divided in 23 patients. In 3 of these for special reasons lysis of these granulations was carried out bilaterally.

Approximately half of these cases showed no physiological disturbance at all following the division of the superior communicating veins leading into the superior longitudinal sinus. Approximately half of the cases showed temporary weakness of the contralateral extremities and a few cases showed transient aphasia. This disability followed in degree from very slight to complete paralysis and complete aphasia: but in no instance did this disability last longer than two to three weeks. These cases have all been followed closely since operation and are in all essential respects neurologically negative. One or two of

Miss Diana Kinloch Beck: In the experimental work to be described, Dr. Dorothy Russell and I have aimed at establishing, by some means, a spreading thrombophlebitis originating in the superior longitudinal sinus.

Despite certain authoritative statements to the contrary the experimental production of thrombosis in the peripheral veins has been shown to be quite a difficult problem but it might be supposed, from a consideration of certain well-known anatomical and physiological peculiarities of the superior longitudinal sinus and its tributary veins, that efforts to produce thrombosis therein would be comparatively easy.

So far as we are aware, only one attempt has been made in this direction. In one dog, Bize (1931) occluded the torcular Herophili and hind end of the superior longitudinal sinus with a tampon of iodoform gauze, and in a second dog he injected 1 c.c. of quinine urethane solution at the same site; in neither experiment was there any significant consecutive clinical or pathological change.

We have attempted by the following measures to induce thrombosis in the longitudinal sinus in rabbits, cats and dogs with remarkable lack of success.

(1) *Inducement of stasis* in the rabbit by occlusion of the lumen at one (four experiments) or two points (three experiments). No thrombosis was found after survival for periods varying from two days to three weeks. We did not anticipate that this would be effective but considered that any possible effects of occlusion should be gauged before proceeding further.

(2) Combination of this procedure in the rabbit with *the injection of coagulants* into the lumen: (*a*) A physiological coagulant: thrombin (five experiments); (*b*) a chemical coagulant: ethamolin (nine experiments).

In practice up to 0·1 c.c. of the coagulant was slowly injected into a segment of the sinus, occluded at either end for a period of two minutes. The dilutions of the thrombin used, though effecting coagulation *in vitro*, produced no effect *in vivo*. The ethamolin though not the thrombin, invariably produced thrombosis, in precisely similar circumstances in the marginal vein of the rabbit's ear, but failed to act similarly in the superior longitudinal sinus.

Repetition of the ethamolin injections in the dog (three experiments) similarly failed in their object.

(3) *Heat coagulation* (two experiments).—In two dogs the dorsal well of the sinus was cauterized down to the intima over segments measuring 0·4 and 1·5 cm. respectively. Examination after four and six days showed no thrombosis beyond minute fragments in the adjacent lacunæ.

(4) *Mechanical blockage of the lumen* in dogs.—(*a*) *By muscle*: A portion of the temporal muscle, beaten into a small "stamp" was introduced (two experiments) through a small opening in the dorsal wall of the sinus by traction on an attached thread. The hæmorrhage incidental to this manœuvre was immediately arrested on the entry of the muscle into the lumen. Although such muscle stamps are powerful hæmostatic agents in neurosurgical operations, they failed to effect thrombosis in these experiments. We therefore, in a further series of four dogs, steeped the muscle in ethamolin for twenty to thirty minutes before inserting it into the sinus in order to injure the endothelium. No difference in effect was obtained. The muscle underwent organization and recanalization in the course of three months.

(*b*) *By cotton-wool soaked in ethamolin* (three experiments): It was considered that blockage by a foreign substance, such as cotton-wool, might effectively occlude the sinus for a longer period.

In two of our animals slight dilatation of a lateral ventricle was found to coincide with a maximal blockage of the sinus (2·5 cm.). Though this asymmetrical dilatation was not impressive we felt it would be worth while to block an even greater length.

(5) For this we selected very young animals in view of the high incidence of sinus thrombosis in young subjects. A further advantage lay in the circumstance that the sutures in these animals were still open.

We succeeded in getting litters of young puppies and kittens aged 6 to 8 weeks. By using two elongated pledgets of ethamolinized cotton-wool, and passing these both fore and aft from a central point of entry on the fully exposed sinus we succeeded in obliterating lengths varying from 1/2 to 5/6 of the whole longitudinal sinus.

TABLE.

PUPPIES			KITTENS		
Aged 6 to 7 weeks Survival 5 to 10 weeks (1 died 36 hours after operation)			Aged 6 to 8 weeks Survival 5 to 7 weeks		
Length S.L.S.	Proportion occluded		Length S.L.S.	Proportion occluded	
4·2 cm.	5/6		4·3 cm.	4/7	
5·5 cm.	2/3		3·8 cm.	1/2	
6·0 cm.	2/3		3·7 cm.	2/3	
5·8 cm.	7/12		4·2 cm.	5/7	

them have had follow-up pneumo-encephalograms which have failed to show any alteration in the size of the ventricle on the operated side.

I do not know how to reconcile this experience with those reported by previous speakers. It should be pointed out, however, that in the cases which I have described, the occlusion of the veins was localized and probably not accompanied by thrombosis for any distance proximal to the ligature. This would facilitate the establishment of collateral circulation which, of course, would be impossible where thrombosis had been extensive.

Dr. Dorothy S. Russell: The uncertainty that still exists concerning the pathology of "otitic hydrocephalus", warrants the recording of the following case.

Clinical.—E. P., male, aged 15, factory worker. He complained, on November 8, 1938, of headache, vomiting and fever of sudden onset. Right otitis media was suspected but myringotomy was negative. On account of increasing drowsiness he was admitted to the London Hospital on November 26. On examination he appeared pale, ill and wasted. There was tenderness over the frontal sinuses, especially on the right side.

Nervous system.—Papilloedema equivocal. Left pupil slightly larger than the right, both reacted sluggishly to light, but fully on convergence. There was a concomitant squint due to weakness of the external recti. The other cranial nerves were normal, though one observer recorded weakness of the left facial muscles. There was weakness and wasting of the left upper limb, especially dorsiflexion of the wrist, and he complained of pain on hyperextension of the left fingers. There was weakness and slight spasticity of the left lower limb, most marked at the extremity. Thus there was almost complete paralysis of abduction of the foot and dorsiflexion of the ankle. The tendon reflexes were elicited as follows: supinator, right absent, left present; knee-jerks, both absent; ankle-jerks, right just present, left brisker; plantar responses, both sides flexor though at a later date (unspecified) the left became extensor. Astereognosis was recorded, but sensation was otherwise unimpaired. Kernig's sign was positive.

Further physical examination revealed bilateral pleural effusions and ascites, the result of extensive tuberculous infection.

Lumbar puncture on the day of admission yielded 20 c.c. of clear fluid under a pressure of 220 mm., containing 20 mg. of protein per 100 c.c., approximately 1 cell per c.mm.; chlorides (as NaCl) 680 mg.%; Wassermann reaction negative. Specimens withdrawn on December 6 and 22 were both sterile on culture.

Progress.—On November 30 the astereognosis had disappeared and there was improvement in the tone in the left upper limb and more power in the lower limb though there was still great weakness of the foot. The papilloedema had increased. Lumbar puncture yielded fluid under a pressure of 300 mm. On December 20 papilloedema had further increased, especially in the right eye. On December 28 a special examination revealed no sign of disease in the right ear, nor in the other air-sinuses. By January 4 the papilloedema had decreased, and at some date (unspecified) the 6th nerve palsy disappeared. The general condition of the patient steadily deteriorated and death took place on January 18, ten weeks after the onset.

Necropsy.—The subject was a greatly wasted, well-developed boy, in whom death was due to perforation of a tuberculous ulcer of the ileum. Organizing thrombus occupied the whole length of the superior longitudinal sinus and the right lateral sinus in continuity. In the latter there was macroscopic evidence of recanalization. The remaining dural sinuses appeared normal. Ante-mortem thrombus extended into many superficial veins over the cerebral convexities. There was no flattening of the convolutions and the leptomeninges appeared normal save for rusty pigmentation about the thrombosed veins. No excess of fluid was observed on the surface of the brain. On section a sharply defined area of greyish-brown necrosis, measuring 1·5 by 1·2 by 1 cm., occupied the hind end of the right superior frontal convolution (*see* fig.). The ventricles were slightly and symmetrically dilated, including the 3rd ventricle (*see* fig.). The aqueduct and 4th ventricle were not demonstrably dilated; the foramina in the latter were all patent. No evidence of tuberculous inflammation was found within the cranium. The right middle ear was moist; other accessory air-sinuses were normal.

Microscopic examination showed that organization of the thrombus in the right lateral sinus was more advanced than in the superior longitudinal sinus and recanalization was confined to the former. The arachnoid villi appeared normal and were not involved in the thrombosis. The hæmorrhagic infarct in the right frontal lobe was enclosed by a zone of foam-cells and macrophages containing pigment granules. Outside this there was a further zone of early gliosis. The thrombus in the adjacent cerebral veins showed early stages of organization. Examination of the medulla oblongata and 4th ventricle through the foramina of Luschka revealed no histological abnormality.

Comment.—In this case we have evidence that aseptic sinus-thrombosis, presumably of the so-called marantic type, began in the right lateral sinus and spread backwards into the superior longitudinal sinus. The left-sided paresis was accounted for by the parasagittal hæmorrhagic infarct in the hind part of the right frontal lobe. This paresis was present on admission to hospital, eighteen days after the onset of the illness. At that time the papilloedema was equivocal and the pressure of the cerebrospinal fluid but slightly raised. A few days later, however, papilloedema had definitely increased and the cerebrospinal fluid pressure was further raised. It would seem that the intracranial condition was improving when death took place from another cause. The subsidence of neurological signs may be correlated with recanalization of the thrombus. The possibility must also be entertained that ventricular dilatation likewise was on the wane at the time of death.
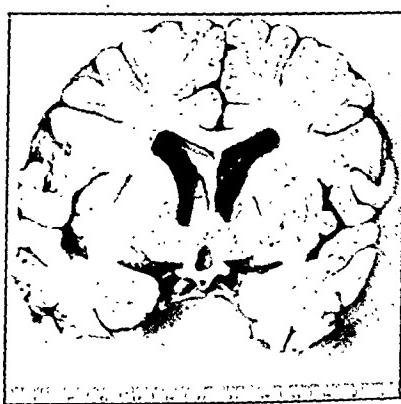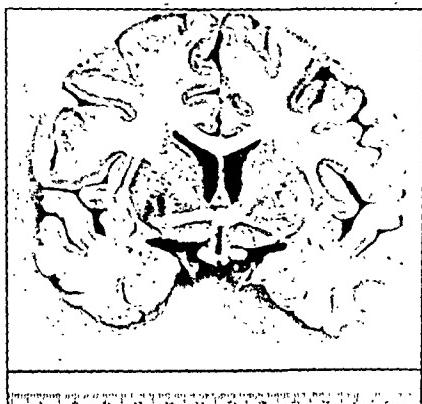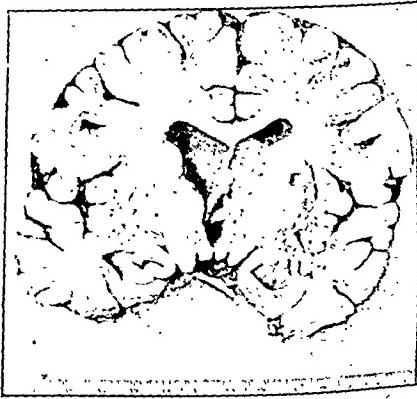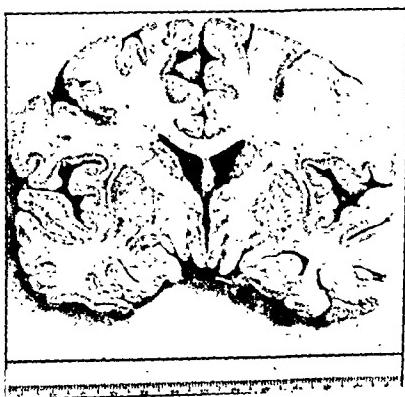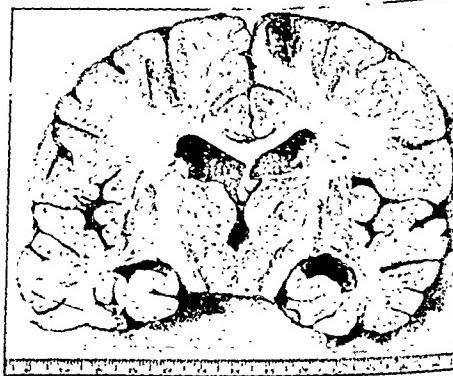
Coronal sections of brain with corresponding level from a normal control arranged on left. Note ventricular dilatation and infarct in right frontal region in lowest section as described in text.

(Dr. Dorothy Russell's case

tract) and terminates in the grey matter in the floor of the interpeduncular fossa. It seems not improbable that such an optic connexion also exists in higher mammals, but efforts to establish it with certainty in carnivores, ungulates and primates have hitherto proved negative.

A great deal of work has been carried out in recent years on the structure of the lateral geniculate body. In man and the higher primates it consists of 6 cell-laminæ, and it has been proved by experimental methods that crossed optic fibres end in layers 1, 4 and 6 while uncrossed fibres end in layers 2, 3 and 5. Thus the crossed and uncrossed fibres are segregated at their termination in the geniculate body, and the most detailed histological studies indicate that there is no mechanism which permits of the fusion of retinal images at this level of the visual system. By noting the distribution of the transneuronal atrophy which follows small retinal lesions, some years ago Mr. G. G. Penman and I were able to show that the topographical representation of the retina into the geniculate body is of a very precise order indeed, amounting practically to a point-to-point projection. It was also found that the smallest retinal lesion capable of producing demonstrable changes in the geniculate body always led to atrophy affecting all three cell-laminæ related to the operated eye. It can be inferred from this observation that the conducting unit from the retina to the geniculate body is a 3-fibre unit. The significance of this is obscure, but I have speculatively suggested that it may be related to the trichromatic theory of colour vision which postulates three kinds of receptor in the retina, responsible for the three fundamental colour sensations.

As regards the exact nature of the connexions of individual optic fibres in the geniculate body, experimental studies with a specialized silver technique have shown that in the monkey each fibre, after entering its appropriate cell-lamina, breaks up into 5-6 terminals each of which ends in a minute bouton applied to the cell-body of one geniculate cell. Each cell has only one such terminal in synaptic relation with it, and thus there is no overlapping of terminals. This disposition clearly provides for the greatest precision in the recording of a retinal image at the geniculate level, and it is interesting to compare it with the condition in the cat. In this animal, large numbers of terminal boutons are related to each cell, and there is considerable overlap in the termination of the optic fibres. While such an arrangement is hardly compatible with precise definition, it does provide an anatomical basis for a high degree of sensitivity even in low degrees of illumination.

It should be noted that complete destruction of one occipital lobe is followed by complete cellular atrophy of the homolateral geniculate body. This seems to make it certain that the cells of the geniculate body project entirely on to the visual cortex of the same side, and leaves no ground for the assumption of geniculo-mesencephalic connexions (as postulated by some authorities), or for a crossed connexion between the geniculate body and the visual cortex of the opposite side to account for macular sparing in occipital lobe lesions. Small, localized lesions of the visual cortex lead to small localized patches of cell atrophy in the geniculate body; hence it appears certain that the point-to-point representation of the retina on the geniculate body is carried on with the same precision through the optic radiation to the visual cortex. The topographical representation of the retina on the visual cortex as established experimentally has been abundantly confirmed by the study of clinical material in which localized damage to the occipital lobe is present. Another point worth noting is that the smallest cortical lesion which leads to a demonstrable atrophy in the geniculate body always involves cells in all six of its layers. In other words the conducting unit of the optic radiation is apparently a six-fibre unit, and impulses from corresponding regions of the six cell-layers are brought into intimate relation with each other as soon as they reach the visual cortex.

Mention may now be made of recent work on the association fibres of the visual cortex, for a knowledge of this system seems to be essential for an intelligent study of the disorders of visual association which follow injury to the cortex surrounding the area striata. Indeed, it is to be hoped that clinicians will focus their attention on localized lesions of this type, since they are likely to throw considerable light on the anatomical mechanisms underlying visual perception. Experimental studies with the application of the Marchi technique, and of the method of "strychninization" of the cortex, have shown that in the primate brain the visual cortex is not (as hitherto supposed) connected by long association fibres with distant areas of the cortex. On the contrary, the association fibres are very short. From the visual cortex itself they extend out into the narrow zone of cortex immediately surrounding it (area 18) and no further. From area 18 other short association fibres extend back to the visual cortex, and forwards to a second narrow zone, area 19, but no further. Area 19 has proved to be one of the "suppression bands" recently

Mr. D. W. C. Northfield : It is difficult to establish the correct diagnosis between cerebral thrombophlebitis and cerebral abscess in cases in which there is a primary paranasal or ear infection. Here are three recent cases: In the first, diagnosis was thrombophlebitis of the anterior part of the sagittal sinus, and cerebral veins, there being an indubitable intra-cranial spread of infection from frontal sinusitis and osteomyelitis. Ventriculography demonstrated a space-occupying lesion of the left frontal lobe, and extensive exploration of the brain by needling on two occasions failed to reveal any brain abscess. Ultimately four abscesses were found and successfully removed from this region; I realise that I might have caused these by the needling. In another somewhat similar case, the right frontal lobe was explored for abscess secondary to frontal sinusitis by a craniotomy, and only swollen brain was found. A few days later the wound was reopened, for fear that an abscess had been overlooked. The veins appeared normal, again no abscess was found but the brain was so swollen that the bone flap had to be sacrificed. The patient made a gradual recovery and has remained well. In a third case, a patient developed symptoms and signs following the extraction of a tooth, of involvement of the right occipital lobe by an expanding lesion. A diagnosis of thrombophlebitis was at first considered, but as the patient's condition was deteriorating, an exploratory craniotomy was performed. Thorough needling of the brain failed to reveal an abscess, and the original diagnosis appeared sound. At post-mortem a few days later, a small abscess was found in the tip of the occipital pole. I should be grateful for guidance in the differential diagnosis.

Dr. Symonds, in reply to Mr. Northfield, said that thrombophlebitis not uncommonly provided a channel of infection which led to the development of a cerebral abscess. This complication should, therefore, be suspected in every case of cerebral thrombophlebitis. A useful point in his experience had been the examination of the cerebrospinal fluid. In the early stages of thrombophlebitis there might be a pleocytosis with slight rise of protein which tended as a rule to clear up quickly. A persistent or increasing abnormality in the cerebrospinal fluid suggested abscess formation.

[*March 2, 1944*]

DISCUSSION ON THE VISUAL PATHWAYS

Professor W. E. Le Gros Clark : In the study of visual disturbances[1] there are a few anatomical points concerning the visual pathways which deserve consideration.

The optic nerve in man contains about 1,000,000 fibres. These fibres vary in size and this denotes a variation in the speed of conduction of retinal impulses. The functional significance of the fast and slow conducting optic fibres is not definitely known, but at least it may be inferred that a timing factor is involved in normal visual processes, and it is possible, therefore, that disturbances in this timing factor may be associated with some types of visual dysfunction. It has been shown in the cat that retinal impulses to the lateral geniculate body are conveyed by the coarse, fast-conducting fibres, while those passing to the mid-brain centres are fine and slow-conducting. Indeed, the rate of trans-mission in these two types of fibre is so different that an optic impulse can be relayed by the geniculate body to the visual cortex, and then down to the mid-brain by cortico-tectal fibres, before it has reached the mid-brain directly. Thus it is theoretically possible for mid-brain reflex activities to be anticipated and modified by cortical influences initiated by the same retinal stimulus.

Direct optic connexions with the hypothalamus have been described from time to time. There is no doubt, however, that many statements which have been made concerning such connexions have been based on inadequate evidence or on the misinterpretation of histological material. For example, fibres have been stated to leave the optic chiasma and to pass upwards and backwards into the region of the tuber cinereum. Experiments made in my own laboratory have shown that this so-called "hypothalamic root" of the optic tract is probably nothing more than an aberrant chiasmal fasciculus which, after passing upwards towards the hypothalamus, loops downwards again to join the optic tract of the opposite side. In lower mammals (rodents and marsupials) a connexion with the hypothalamic region or its immediate neighbourhood certainly does exist by way of a fasciculus called the posterior accessory optic tract, which leaves the main tract near the lateral geniculate body, crosses obliquely the crus cerebri (as a part of the transpeduncular

Various explanations have been put forward to explain the macular escape that may occur in hemianopia of cortical origin. Some have attributed it to representation of each side of the maculæ in both occipital lobes by way of fibres which branch in the chiasma, or to some of the fibres of the radiations crossing to the opposite side through the corpus callosum. The completeness of the hemianopia due to lesions of an optic tract excludes the first hypothesis. Decussating fibres from the radiations, as has been assumed by the second hypothesis, have never been demonstrated, and the fact that retrograde changes are not found in the opposite external geniculate ganglion after destruction of one occipital lobe excludes their existence. The hypotheses of representation of the maculæ outside the area striata, or their projection both posteriorly and anteriorly within it, have not been based on adequate evidence.

The macula is the most highly evolved and differentiated portion of the retina and has consequently, in relation to its size, an enormously greater cortical representation than its periphery; it frequently extends over the pole of the occipital lobe on to the lateral surface of the hemispheres, and it is therefore less likely to be completely destroyed than other parts of the visual cortex. It lies in the margins of the distributions of the middle and posterior cerebral arteries and when one of these is occluded a portion of it at least may receive sufficient blood from the other to remain functional. This is the probable explanation of macular escape in cases of cortical thrombosis, and of the retention of macular vision in many cases of bilateral hemianopia.

Fuchs has pointed out that in some cases of hemianopia the subjective visual field is shifted towards the blind side so that the patient uses in fixation not the normal fovea, but a pseudofovea to its seeing side, and thus obtains a greater field of vision. If this should occur the blindness would not reach the fixation point and a field presenting macular sparing would be obtained. Vision along the vertical meridian should also escape, as it sometimes does in homonymous hemianopia.

The formation of a new point of central vision appears *a priori* improbable, but it must be remembered that in certain cases of squint a false macula which provides more distinct vision than the true fovea may develop. This can be due not to functional changes in the retina but to physiological adaptations in the cortex; the cortex is essentially a plastic organ in which function is not so rigidly bound up with structure as in more highly organized lower levels of the nervous system.

The development of a pseudofovea in Fuchs' sense is not offered as a hypothesis to explain macular sparing, but its possibility has to be considered in interpreting abnormalities in the visual fields due to cortical lesions.

Major J. W. Aldren Turner : *Indirect injuries of the optic nerve and chiasm*[1] [Abstract]. —These conclusions are based on a study of 50 cases of optic nerve injury and 3 of chiasmal. In a consecutive series of 1,550 head injuries the optic was the third most frequently damaged cranial nerve. The position of impact to the head in these cases is almost invariably in the frontal region, unlike olfactory nerve injuries where an occipital impact is almost as frequent as a frontal one.

There may be unilateral blindness for two to three days after injury even when considerable return of vision will take place later. Improvement usually starts about the third or fourth day and further recovery after the end of the fourth week is exceptional. In minor injuries of the nerve normal visual acuity may return. The visual field defects are of two types, the first where a scotoma is the prominent feature and the second where a sector defect in the peripheral field is found, but some overlap between these two types occurs. There is usually no change in the fundus in the early stages but in severe injuries optic atrophy appears in about three weeks; in the minor injuries pallor of the disc may never become noticeable. There is no change in size of the pupils in an uncomplicated optic nerve injury.

X-rays of the optic foramina taken in 41 of these cases showed an abnormality in only 5 of them, in 2 a fine fissure extending into the foramen and in 3 an irregularity of the wall of the foramen suggestive of trauma.

Injuries of the optic chiasm are much rarer than those of the nerve—the site of impact is usually frontal—the field defect is a bitemporal hemianopia of varying degree, the visual acuity depending on the relationship of the field defect to the fixation point. Diplopia without weakness of the external ocular muscles may occur as a result of the attempt to use non-homologous portions of the two retinæ.

[1]*See* J. W. Aldren Turner (1943) *Brain*, **66**, 140.

described in the cerebral cortex. Stimulation of this area has the remarkable effect of suppressing the normal electrical activity of the entire cortex, and there is good evidence that this is mediated by fibres passing to the basal ganglia, whence inhibitory impulses are relayed via the thalamus or hypothalamus. Thus it may be inferred that when retinal impulses are finally relayed to area 19 (and not till then) they arrive at a point where they can influence the activity of the brain as a whole.

The last point which I should like to mention in this brief contribution concerns the pathways of the optic fibres which are involved in the pupillo-constrictor reflex. For a long time it had been accepted that the superior colliculus is an essential link in this pathway, but it has now been definitely established that this is not so. On the contrary, the afferent side of the reflex arc has been shown to consist of optic fibres which terminate in an element called the pretectal nucleus, which is situated under cover of the antero-lateral margin of the colliculus. Here the fibres synapse, and relaying fibres convey the impulses directly to the oculomotor nucleus of the same side or across the posterior commissure to the opposite nucleus. It still remains a mystery why these fibres are selectively involved in the production of an Argyll-Robertson pupil. The explanation, once current, that it is because they are unmyelinated and therefore more vulnerable is certainly incorrect. According to Arey, there are no unmyelinated fibres in the human optic nerve.

Dr. Gordon Holmes: Till 1914 the exact topography of that portion of the cerebral cortex which receives visual impressions directly was uncertain. Henschen had, by collection and analysis of a large number of cases in which disturbances in the fields of vision were associated with lesions of the occipital lobes, made it probable that the visual receptive area coincides with the area striata, but projection of the retina within it was not definitely ascertained; some authorities, for instance, placed macular representation anteriorly, others posteriorly. The last European war provided opportunities for investigating the effects of local injuries of the occipital lobe and made it possible to construct a map of the projection of different portions of the retinæ on the cortex. It was placed beyond doubt that the maculæ are represented posteriorly in the area striata, the peripheral portions of the retinæ anteriorly, the upper segments in its upper and the lower in its lower or ventral part. Further, it appeared probable that the vertical sectors of the retinæ adjacent to the vertical meridians correspond to the portions of the area striata exposed on the medial surface of the hemispheres, and the horizontal sections to the cortex lining the depth of the calcarine fissure. Subsequent clinical, anatomical and experimental observations have confirmed the conclusions arrived at by these investigations on the visual disturbances which result from gunshot wounds. There therefore seems to be an intimate point-to-point projection of the retinæ in the cortex.

The striking feature of the effects of local injuries of the cortex is the permanence of the defects in the fields of vision. In one case, cited as an example, a small paracentral scotoma, observed about two weeks after infliction of the wound, remained unaltered for at least four and a half years.

Certain problems in the organization of the visual cortex remain, however, unsolved. Isolated loss of colour vision in the whole or parts of the homonymous halves of the fields is frequently reported and has led to the assumption that the perception of colour is mediated by certain layers of the cortex, or is localized outside the area striata. In my experience visual acuity for whole light is always reduced in areas in which perception of colour is defective. A small group of cases in which the predominant feature is the condition described by Dejerine as "Pure Word Blindness" is an exception, as in many of those which have been recorded the patient was unable to name or match colours, and in some colour memory was defective. In all these cases in which it has been verified, the lesion lay in the basal surface of the temporo-occipital lobe, usually in the left side. This condition is, however, a colour agnosia, not loss of colour vision as such.

The explanation of "macular escape" or "macular sparing" in certain cases of homonymous hemianopia has been a subject of considerable controversy. According to certain authors it occurs only when the visual cortex is destroyed, never with lesions of the geniculo-striate fibres or optic radiations. This certainly does not correspond with my experiences, for I have often observed that the blindness did not reach the middle line in the region of the fixation point when the radiations were injured either in the internal capsule or in the substance of the hemisphere, and in a large number of instances of local injury of the cortex I found that the loss of vision, in the form of either hemianopia or local scotomata, extended exactly to the fixation point. I have been able to ascertain in several cases that this loss of vision without macular escape may be permanent. Further, I have seen loss of central vision in each eye due to destruction of both occipital poles.

Section of Orthopædics

President—S. Alan S. Malkin, F.R.C.S.Ed.

[*March* 7, 1944]

Experiences as a Prisoner of War in Germany

By Major W. E. Tucker, R.A.M.C.

This short paper describes the places where we worked in Germany, the food conditions, surgical instruments and equipment and the types of orthopædic cases we had to treat during our three and a half years' sojourn.

I realize that there have been great advances in the orthopædic field since 1939, but it has been impossible for me since my return to cover all these and therefore some of the points I stress may appear obvious and of general knowledge to orthopædic surgeons.

I was captured at Camiers near Le Touquet on May 23, 1940, where we were left with 200 wounded. We remained there for seven weeks, during which time some 1,500 wounded, both British and Dominion, passed through our hands. From there we were evacuated in the middle of July to the buildings of the Université Catholique in Lille, where the number of wounded amounted always to between 500 and 600.

At the beginning of October we were transferred with our wounded to Enghien, southwest of Brussels, where we found three other British medical officers with British wounded. We were there for a month and finally before proceeding into Germany we were ten days at Malines on the north-east side of Brussels.

In early November a good ambulance train took us and our wounded into Germany, where I was fortunate enough to be employed over the whole period in hospitals with our wounded. We spent ten months in Dieburg, near Frankfurt am Main, and just over two years at Obermassfeld in Thuringia. During the last year I paid a monthly visit to the hospital at Klosterhaina, where the amputation cases and other orthopædic cases were sent for rehabilitation from IX C area and other camps, and I went for a month to Schildberg in Poland in order to examine and give advice on some 600 orthopædic cases there, who had already passed the International Commission for repatriation.

I will now describe two aspects of hospital life: The food and the surgical facilities available.

Soon after we were captured our daily ration amounted to not more than 1,200 to 1,300 calories a day. Naturally we medical officers lost weight, but it was worse for the orderlies, who had to do a great deal of heavy manual work, lifting and carrying. For the patients who were suffering from fractures, gross sepsis, septicæmia, &c., this was a starvation diet and gave them no chance of picking up. The effect of food was shown in our last week at Camiers, when most of the hospital had been evacuated to Lille, except for five medical officers and 68 of the most seriously ill patients. We were then allowed to eat the remainder of our food stores and we proceeded to have a good week's tuck-in with at least 3,500 calories a day. The 68 patients immediately picked up and on our arrival at Lille with them we noticed their marked improvement compared with those already there. In Lille the diet ration continued to be about 1,300 calories a day for the first ten days, but soon owing to the generosity of the French and Belgian Red Crosses we were able to supplement this considerably, but even so I do not think our daily intake amounted to more than 2,000 calories.

After three months in Germany with the arrival of the Red Cross parcels, the food situation improved tremendously. Previous to their arrival we experienced having to work on a diet of about 1,500 calories a day, but with the addition of the Red Cross

[The views as to the method of production of optic nerve injuries were discussed and it was concluded that an intraneural vascular accident resulting from violent impingement of the nerve against the wall of the bony optic canal was the most probable mechanism. (Traquair, H. M., Dott, N. M., and Russell, W. R. (1935), *Brain*, 52, 398.)]

Mr. E. B. C. Hughes : It is a curious fact that in traumatic and compressive lesions of the optic chiasm and of the optic nerves, the upper nasal quadrant of the visual field is frequently spared. In cases of optic nerve injury in which total loss of vision has been present at first, if recovery takes place it most commonly commences in this upper nasal quadrant. It is well known, of course, that in tumour cases and in traumatic lesions of the optic chiasm, the upper nasal quadrants are frequently spared until late. This observation has been made so often that it has led Traquair to suggest that it is possible that the fibres subserving the lower temporal quadrant of the retina may have some peculiarity of their blood supply which makes them less vulnerable to injury.

With regard to closed injuries of the optic nerve, Major Aldren Turner and others have stressed the fact that in the early stages the fundus picture is normal. This I have not found to be the case, and in most of the early cases that I have examined, I have found disturbance of the retinal vascular tree, usually confined to spasm of one or more branches of the central retinal artery, but on occasion affecting all branches and giving the fundus a picture indistinguishable from that of central artery thrombosis. In the majority of such cases that I have observed over a period of time, the vascular picture of the retina has returned to normal within a few weeks, regardless of the fact that vision and the visual field may have shown no improvement. One case in particular was most striking:

Examined within a few hours of injury, this showed spasm of all the retinal vessels, with commencing œdema of the retina. Explored at operation by Mr. Harvey Jackson within twenty-four hours of injury, the entire optic nerve from globe to chiasm was examined and appeared completely normal. Within six weeks the retinal vascular pattern had returned to normal, but there was still no perception of light in that eye, and the disc showed severe primary optic atrophy.

and muscles over the bone and rest in plaster for a month, that a great deal of time was often saved by complete saucerization of the wound provided the general condition of the patient allowed it. This certainly applied to the later cases in which gross sequestra were present. It was my opinion that not only was it necessary to saucerize the bone, so that the involucrum of one side was removed, but that quicker and better healing took place when a large amount of skin, deep fascia and even muscle were removed as well. The results of removal of large portions of the vastus lateralis or biceps femoris in osteomyelitis of the femur were excellent and showed remarkably little loss of power of knee extension or flexion after three to four months.

In some cases after the removal of the involucrum on one side of the bone, it would be necessary, when new bone growth was sufficient to ensure that the bone would not fracture, to remove the involucrum on the other side as this remained infective and prevented healing.

In some cases in which the radiograph shows osteoclerosis it is probably better to pick out sequestra, if sequestra are present, or one can wait and see whether in the dense bone small sequestra begin to show when radiographed, in which case they can be picked out or allowed to discharge themselves.

In some cases with persistent sinuses it was found on radiograph that there was a hole through the shaft of the bone. At one time I tried the effect of plugging the holes with muscle grafts when swabs taken from the wound showed no growth of organism. I soon abandoned this procedure in favour of complete saucerization of the wound, which necessitated removal of the bridge of bone nearest the surface. This allowed the soft tissues to collapse and thus obliterate the hole.

Nerve injuries.—Many of these cases were not sutured, as gross sepsis persisted, making it impossible, and also we never knew exactly when the wounded were not going to be repatriated. Major Henderson sutured 30 to 40 cases at Schildberg and I did the ones at Obermassfeld. We found that in some cases where at first suture appeared impossible, it was possible to perform it if the operation was performed in two stages. The first stage consisted in mobilizing the ends, transplanting if necessary and suturing the damaged ends with the joints flexed to make apposition possible. Gradually the joint was extended and in three to four months a second operation was performed, damaged nerve removed and, with the lengthening obtained by further mobilization and the stretching of the nerve by the previous gradual extension of the limb, suture would be possible.

In many cases of peroneal palsy, apparent paralysis persists due to the stretching of the dorsiflexors and evertors of the foot by the weight of gravity, and the action of the more powerful plantar flexors and invertors, when the nerve has really recovered as shown by return of faradic response in the peroneal and anterior tibial muscles. It is difficult also in these cases to overcome the patient's habit of walking with a drop-foot gait. I think that we should be more careful in discarding the necessary apparatus for this deformity, allowing it off only for so many hours each day at first and at the same time persisting with supported non-weight-bearing dorsiflexion and eversion exercises and faradism. A metatarsal bar placed between the layers of the sole of the boot helps.

I noticed that Professor Seddon advises in cases of musculospiral injury the removal of the cock-up splint for a short period each day. With this I can strongly concur as the normal extensibility of the extensors is maximum with the wrist-joint metacarpophalangeal and interphalangeal joints flexed, and if the cock-up splint supports the wrist and metacarpophalangeal joints continuously this normal extensibility is interfered with and the patient cannot make a full fist. It is interesting to note in these cases that there are no adhesions in the metacarpophalangeal joints preventing a full fist and it seems that the extensor tendons themselves have shortened.

Contractures.—Wounds of the popliteal space lead to persistent flexion of the knee with subsequent flexion contraction. We found that any form of traction established to prevent this only led to increased pain, rise of temperature and inguinal adenitis and the extension had to be removed. Whether this was due to insufficient wound drainage or obstruction to lymphatic and venous return I do not know. The fact remained that we just had to allow these cases to contract, but we found that with time, i.e. over two years, gradual stretching of the contracted structures took place and no operative interference was indicated and, as the wounds had been so grossly contaminated, was actually contra-indicated.

Stiff joints.—It is imperative to appreciate two types: (1) Those with adhesions alone; (2) those with adhesions plus a large amount of infiltration with lymph and old hæmorrhage from injury or inflammation from sepsis. Naturally most of our cases fell into the second category.

parcels we were able to supplement this with about 1,200 extra calories a day. During the last two years with the excellent invalid comfort parcels and blood transfusion facilities the patients undergoing extensive sequestrectomies, amputations, &c., I must say, were able to receive as excellent after-care as they would have in any British hospital at home. Our instruments, on the other hand, were the merest essentials.

We started with three dozen pairs of Spencer Wells forceps, and these with the rest, such as chisels and osteotomes, were under constant use for over three years. Except for an occasional replacement through the Red Cross and German authorities we had to manage with these. To be fair, during the last year the Germans tried to produce a few extra orthopædic requirements such as Balkan beams, Braun Splints, but they themselves were terribly short and many of the things we asked for just could not be produced. Repairs of instruments through the Germans took from six to nine months. Although we were supposed to be an orthopædic hospital we had no extension table, no drill or electric saw and one Thomas' splint. We managed for spica plasters with a pelvic rest, orderlies and continuous traction. For a drill we used the carpenter's brace and bit.

Throughout, our theatre facilities were not too bad and we could be certain of having sterile instruments and dressings for the operations, but for the after-dressings we had to depend almost entirely on antiseptic dressing and sulphonamide powder. We were lucky in having Major Challis, Major Steele and Capt. Odell as anæsthetists, which made all the difference.

Our patients came under the following types: (1) First type: Battle casualties wounded longer than eighteen hours and in most cases four to seven days. Except for a few airmen and the ordinary accidents amongst prisoners we saw very few recent cases; therefore our surgery consisted mainly in opening up wounds to promote free drainage, removal of clot and damaged muscles and removing foreign bodies, "débridement" in distinction to "excision of the wound" or "épluchage". On the whole the surgery of these cases had naturally to be on the conservative side, as they were in that between period where too drastic surgery would have opened up tissue planes and broken down the natural defence system of the patient. Consideration of the patient's general condition was one of the most important parts of the treatment.

(2) Later these cases became our second or chronic group of battle casualties. All the wounded men from France, Belgium, Crete and Greece as well as those from Dieppe gradually merged into the chronic group.

(3) The third type of cases were the wounded airmen and during the last year we were treating an equal number of British and Americans in our hospital: about every ten days a batch of 20 to 30 of these airmen would arrive.

Naturally fractures played a prominent part in their disabilities and I found that a Pott's-Dupuytren fracture of the ankle was easily the most common.

For femur fractures we employed extension by a Kirschner wire through the tibia, the leg placed on a Braun Splint and traction up to 30 to 40 lb. for only a few days. The bed would then be wheeled into the theatre, patient anæsthetized, placed on a pelvic rest, the dorsal spine supported by a double mattress biscuit, and with the traction maintained and several orderlies holding, a double plaster spica was applied. The back of the plaster holding the foot and leg was hinged back at the knee so as to allow knee flexion after seven weeks.

We saw remarkably few cases of frost-bite in airmen and this may be accounted for by the fact that those captured had only made a journey one way, instead of to Germany and back to England.

Two of the airmen with frost-bite had been submitted to several days' exposure in the North Sea and had no doubt saved their limbs by keeping them immersed in sea water, thus avoiding cold winds.

(4) The final group included the ordinary orthopædic conditions occurring in a group of some 6,000 to 7,000 prisoners, such as work accidents, sprains, strains, rupture of muscles, flat-feet, whitlows and knee injuries.

During the period of captivity I opened the knee-joint on 25 to 30 occasions for removal of cartilage or loose bodies without a suspicion of trouble, and we never had any sepsis in relation to nerve sutures. We did on the other hand experience a certain amount of trouble with sepsis in cases of appendices and herniæ, especially in the French and Serbs. Considering that at times the hospital was literally oozing pus from cases of osteomyelitis this was understandable. The hospital blanket could be sterilized only about once in every four months, and was passed from patient to patient. We found that other hospitals had the same experience.

Osteomyelitis.—I found that as soon as it was established that infection of the bone was not going to clear up by conservative methods, such as free opening of skin

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*February* 25, 1944]

The Recognition and Palliative Treatment of Early Sinus Trouble in Children

By H. G. BEDFORD RUSSELL, F.R.C.S.

SINUS trouble is common in children, in whom the exanthemata pave the way for streptococcal infection. It would probably be recognized more often if it were realized that effective palliative treatment is possible.

The typical tissue-response to streptococci is production of œdema, not pus. Insistence upon pus for diagnosis of sinusitis has occasioned non-recognition of numerous cases, in which 5th nerve irritation and local absorption along the lymphatics produce symptoms customarily regarded as primary (e.g. "neuralgia") in parts remote from the sinuses.

Dyes absorbed from the sinuses may appear in the urine in twenty minutes, and be recognized also in the brain and in the cervical and upper dorsal musculature.

Tonsillar inflammation is usually a result of sinusitis, as are also otitis media, conjunctivitis, headache, and many types of deviation from normal behaviour.

It is wise to assume that the sinuses are involved in most of the exanthemata, influenza, and pneumonia and to initiate palliative treatment without delay, if chronic inflammation is to be avoided. The most cogent result of acute inflammation of the linings of the sinuses and of the nasal passages is the mechanical difficulty occasioned *at the ostia* by swellings of the membrane in an inexpansible bony ring, which leads to "sinus-block". The indication, therefore, is to reduce the œdema at the ostia so as to permit the normal entry of air into the sinuses and to facilitate the escape of the increased secretion.

FIGS. 1, 2, 3 and 4 show stages in the introduction of lipiodol by Proetz's displacement method.
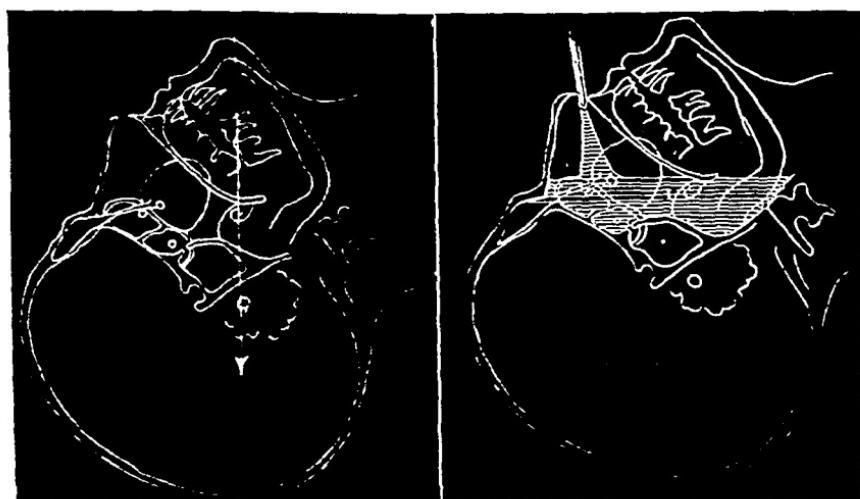
FIG. 1.—Correct position for displacement.　　　FIG. 2.—Indicates relation of fluid level to ostia of the sinuses.

After all evidence of sepsis had subsided these cases were given non-weight-bearing exercises and faradism with regular gentle manipulative movements. It is important to distinguish the difference between gentle manipulative movements and passive movements. We all agree that the term passive movements should be deleted from physical treatment. Gentle manipulative movements on the other hand aimed at stretching contracted capsule, ligaments, and tendons by traction and counter-traction within the range of active movements, and by this means to restore those movements of a joint which are out of the range of voluntary movement but which are so important for painless movement. No force is used and no undue reaction caused. It is essential to promote absorption of the lymph, old hæmorrhage, products of inflammation from sepsis, before a manipulation under anæsthesia is resorted to. Otherwise a violent reaction is caused with further embarrassment to the circulation, and increased stiffness.

Limitation of knee flexion after fractures of the femur.—We had considerable success in obvious stationary cases through injecting isotonic saline into the quadriceps muscles and around the boundaries of the suprapatellar pouch. These injections were followed by gentle manipulative movements of the joint combined with faradism, heat and massage.

X-ray.—We were able to obtain fairly good radiographs of bone except for lateral spines. There were no facilities for screening until just before I left Germany and stereoscopic X-rays were out of the question. For localization of foreign bodies we depended on the introduction of two needles placed under local anæsthesia at right-angles and films taken in two planes. This gave us a rough localization.

Plaster.—The results with the German plaster of Paris were fairly good, except that it took a long time to set. We found there was some chemical in the plaster which caused skin irritation; for this reason we surrounded the skin with paper bandages. For high fractures of the femur we found a modification of the Roger Anderson well leg traction most efficacious. Instead of the Roger Anderson apparatus we used a slat of wood. The two legs were encased in plaster, the sound leg above the knee, the wounded leg below the knee. The slat was first plastered to the sole of the wounded leg and when the plaster was set, traction was applied to the slat in a downward direction by pressure on the slat on the outer side of the wounded leg and counter-traction was established by forcing it up against the sole of the well leg. This method was so successful in making the patient comfortable, and in allowing easy dressing that it was also adopted by the other surgeons. In this apparatus we found that the patient was easy to transport and did not feel the movement unduly. In battle casualties I consider that leg plaster should extend beyond the toes and the plaster then will act as bed cradle. We saw many cases of clawed contracted toes simply due to the weight of the bedclothes.

Rehabilitation.—We divided the classes into the following groups: (1) Exercises for bed patients. (2) Special classes for up-patients: (*a*) upper extremity; (*b*) trunk; (*c*) lower extremity; (*d*) special cases. (3) Fit classes taken by physical training instructor for doctors, orderlies and certain fit patients.

Captain Laurie, who is a lecturer in physical training at Aberdeen in peacetime, volunteered to supervise the rehabilitation at Klosterhaina. There, with the aid of several ingenious workmen, he constructed exercise machines of all types. Thus we were able to give suitable exercises for finger, shoulder, quadriceps, ankle. Great work was accomplished by him and his staff and he made his classes famous in the camp by combining them with interesting games.

Physical methods.—I was fortunate in having with me one of my own masseurs in civilian practice and we were able to supplement exercises with radiant heat, massage, faradism, interrupted galvanism and direct galvanism, short-wave diathermy and ultraviolet light.

I wish to point out that we had many of our patients under control for three and a half years and the time factor was a great help in restoring maximum function; at the same time we were handicapped by lack of instruments in carrying out all the operations, such as bone grafts, that were required. Finally I should like to pay a tribute to the R.A.M.C. orderlies, most of whom started knowing very little, but soon picked up the work and were magnificent throughout.

medium. Rapid alterations in mucosal thickness, suggesting urticaria, are demonstrable in asthma, migraine and epilepsy.

BIBLIOGRAPHY

BIRDSALL, S. E. (1939) Symptoms, Signs and Treatment of Nasal Sinusitis in Children, *J. Laryng. Otol.*, 54, 549.
EBBS, J. H. (1938) A Note on the Incidence of Sinusitis in Children *Brit. med. J.* (i), 385.
GUNDRUM, L. K. (1940) Treatment of Sinusitis by the Displacement Method, Report on 800 cases, *Laryngoscope*, 50, 989.
KERLEY, C. G. (1938) Sinusitis in Children from Pediatric Standpoint, *Arch. Pediatr.*, 55, 732.
PICKWORTH, F. A. (1935) Chronic Nasal Sinusitis and its Relation to Mental Disorder. London.
PROETZ, A. W. (1931) The Displacement Method of Sinus Diagnosis and Treatment. St. Louis.
RUSSELL, H. G. BEDFORD (1939) Observations upon the Nasal Aspect of Asthma, *St. Barts. Hosp. Rep.*, 72, 23.
—— (1942) Observations upon the Nasal Aspect of Mental Disorder. Read before the Royal Medico-Psychological Assoc. at Preston, October 1942.

The Diagnosis and Treatment of Sinusitis in Children

By S. E. BIRDSALL, F.R.C.S.

I HAVE for the past eight years made a systematic study of the problem of sinusitis in children, my cases being chiefly drawn from the large out-patient clinic at Paddington Green Children's Hospital. I recorded in 1939 the clinical features in 80 cases of indisputable sinusitis, and as these were selected particularly because the diagnosis was proven beyond all dispute, it may be confidently assumed that the facts which they illustrate are to be regarded as reliable evidence.

Development.—The developmental continuity of the mucosa of the nose, sinuses and middle ear leads to the logical conclusion that sinusitis is likely to be as common as is otitis media in children. That it is not so regarded is probably explained by the three obvious corollaries of middle-ear disease which make its recognition easy, and which are not found in the sinus infections of children: Pain, loss of function, i.e. deafness, and visible external discharge.

Sinusitis without pus.—It is very rarely that the sinusitis of children is not readily discernible by the ordinary methods of examination, if properly performed.

During eight years I have never allowed myself to fail to examine any child by anterior rhinoscopy. A small speculum is essential, but in children under 3 the anterior nares are greatly widened simply by light pressure on the tip of the nose. The absence of vibrissæ and the short vestibule render anterior rhinoscopy easy in the child.

Posterior rhinoscopy.—Sir StClair Thomson says of children: "Posterior rhinoscopy does not succeed." We should not regard this pronouncement as final. I find that in children posterior rhinoscopy succeeds rather more frequently than in adults, as children with the mouth widely opened still breathe through the nose, and thus maintain the patency of the nasopharynx. Mouth-breathing is rare in children.

Origin of sinusitis.—In my series of 80 cases the ætiological factors were difficult to assess, and in only 13 was there good evidence of an antecedent cause. Of specific diseases, whooping-cough is undoubtedly the commonest, unless we regard the common cold as a specific infection. All the specific fevers except mumps and chicken-pox are common precursors of sinusitis. Sinusitis is probably as common as otitis media as a complication of scarlet fever, and culturally identical streptococci have been recovered from the ear and from the antrum of the same side in post-scarlatinal otitis media.

Symptoms.—The symptoms of sinusitis in children, if considered in a logical way, point to the sinuses as the probable source, though such symptoms are often ascribed to infection of the tonsils and adenoids.

Adenoids.—Nasal obstruction is universally regarded as the prominent and diagnostic sign of hypertrophy of the adenoid tonsil. In fact, it must be extremely rarely that mouth breathing is due to nasopharyngeal obstruction by adenoids. The widest part of the pharynx is that immediately above the pharyngeal orifices of the Eustachian tubes, and diminution of the lumen is less likely here than in any other part to embarrass the airway.

We find that the commonest symptoms leading to a request or even a command for tonsillectomy and removal of adenoids are: Frequent so-called colds, snoring, mouth-breathing (never confirmed by observation), backwardness both physical *and* mental—none of which can logically be attributed to disease of the tonsils or adenoids, or a host

FIG. 3.—Replacement of air by fluid only up to the level of the ostia.

FIG. 4.—Completion.

FIG. 5 shows normal acceptance of oil by antra.

FIG. 6 shows normal acceptance of oil by sphenoids.

This can be achieved by the introduction of non-toxic volatile vaso-constrictors, such as methedrine or benzedrine, or fluids from a fine spray: Neosynephrin hydrochloride in $\frac{1}{4}\%$ solution is the best so far obtainable. Ephedrine hydrochloride, $\frac{1}{2}\%$ in normal saline, is also effective. If the nasal lining is sensitive it is desirable to spray with

Cocaine hydrochloride		4%
Ephedrine		1%
Pot. sulph.		0.5%

[The displacement method was then demonstrated.]

The principle of the displacement method is the partial withdrawal of air from the sinuses with a modified breast-pump, the head being inverted and the nose filled with $\frac{1}{2}\%$ ephedrine hydrochloride in normal saline, the solution replacing the air in the sinuses upon discontinuance of the suction.

Displacement has been found effective, particularly in young children, and is practised at the Metropolitan Ear, Nose and Throat Hospital, Paddington Green Children's Hospital, St. Bartholomew's Hospital, in this country, and extensively in America. Operation is rarely indicated; antral empyemata can frequently be emptied by displacement treatment, which may be repeated with advantage after an interval of five minutes.

Lipiodol, similarly introduced, is valuable in radiological diagnosis. Mucosal swellings, often vaguely indicated in plain X-rays, are clearly shown against the contrast

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*February* 17, 1944]

Cheese Itch and "Itchy Cargoes" in Reference to Workmen's Compensation

By J. A. NIXON, C.M.G., M.D.

[*In Absentia* Read by DR. PROSSER THOMAS]

IN 1915 I was asked to investigate a complaint made by dock-labourers that they were unloading a cargo of cotton-seed which gave rise to an irritating eruption. I found that the cotton-seed was full of a mite known to give rise to such an eruption, namely *Pediculoides ventricosus*. In January 1944 the secretary of the local branch of the Dockers' Union (Transport and General Workers) came to me and reminded me of this and asked if I would investigate another "itchy cargo" consisting of cheese. With the consent of the stevedores I went on to the steamer in question but found the whole consignment of cheese had been discharged. However there was some grain lying about from a previous cargo and a great deal of sawdust in which the cheese had been packed. Otherwise the hold was empty. There chanced to be a railway waggon on to which the cheese was being loaded from a lighter. The cheeses were packed in crates made with slats of wood, which left them easily accessible.

I took scrapings from the muslin covering the cheeses, some of which showed a grey feathery mould. Scrapings from this mould showed that it was swarming with a live mite. This mite was only found in the mould, not in the sawdust, nor the grain from the hold and not in scrapings from the muslin which showed no mould. Dr. A. L. Taylor, Pathologist to the Bristol General Hospital, who has kindly mounted specimens for me and made camera lucida drawings of them, identified the mite as *Tyroglyphus longior*.

This mite was fully described in the *British Journal of Dermatology and Syphilis* (December 1942, p. 313) by Dr. Prosser Thomas.
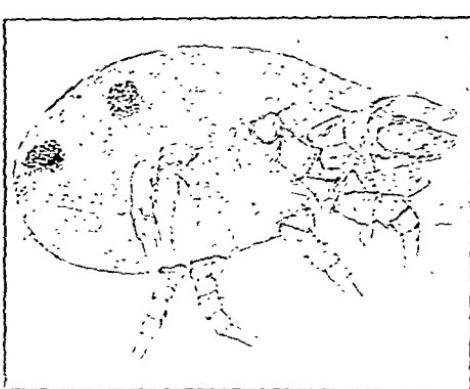
Specimens of Tyroglyphid mite from cheese dust.
(The slides were prepared by Dr. A. L. Taylor, Pathologist, Bristol General Hospital, and the photomicrographs were made by Mr. T. J. H. Cooke, photographic assistant to the Department of Medicine, University of Bristol.)

The effect on the dock labourers was exactly as described by him.

My principal reason for bringing the subject before the Section is to invite discussion on the problem of compensation for the workmen. Occasionally handling of "itchy"

of miscellaneous disorders such as bed-wetting, nose-picking, habit-spasms—including various non-pathological coughs, and even juvenile delinquency!

Mouth-breathing.—This simple composite word is of enormous importance, not because the condition is common, but because it is rare. When it occurs it is a sign of either sinusitis—almost always, or of two very rare conditions—congenital atresia of the posterior choanæ or a nasopharyngeal tumour. A very instructive experience can be enjoyed easily by visiting a children's ward at night. The proportion of children who are sleeping with open mouths will be found to correspond very closely with the proportion whose age is below 6 years, the age at which the mandible begins to grow rapidly to accommodate the permanent teeth. The "mouth-openness" of the small children, mis-named mouth-breathing, is cured by the increasing length of the body of the mandible. Moreover the angle of the mandible, 175° at birth, is reduced to 110° after puberty. Whether the patient is breathing through the nose or through the mouth can be easily determined if the observer will quietly approach with a cold spatula, and hold it beneath the nostrils.

In my own series of 80 cases the symptoms in order of frequency were: (*a*) *Nasal obstruction.*—One-half of the children with this prominent symptom had previously undergone tonsillectomy and removal of adenoids. In only one case was the obstruction due to adenoids. It was usually caused by a combination of mucosal œdema and the presence in the meati of the nose of thick mucopus.

(*b*) *Cough* will occur as a direct consequence of downwardly propelled sinus secretion.

(*c*) *Colds.*—If a child is said to be "never free from a cold" it may be presumed that he has sinusitis. I believe allergic nasal conditions to be very rare in children. The allergic nasal mucosa of adults is in its appearance characteristic, extreme pallor, swelling, and irritability. I have very few notes of its occurrence in children, and do not recollect having recorded it except in hay-fever.

(*d*) *Anorexia.*—This symptom was in definite relation to the magnitude of the suppurative reaction.

(*e*) *Otorrhœa.*—It is my opinion that the vast majority of children with chronic otitis media have sinusitis, and the significance of this conclusion merits a special discussion.

DIAGNOSIS BY EXAMINATION

In the adult, the classical description of pus in the middle meatus of the nose is very often not demonstrable on rhinoscopy. In the child it is usually obvious. Indeed the mucopurulent secretion commonly fills the inferior as well as the middle meatus, and its presence in the normal path of inspired air explains the outstanding symptom of nasal obstruction. The diagnosis is therefore simple. The only other conditions which will thus fill the lower half of the nose with mucopus are nasal diphtheria, foreign bodies, and congenital syphilis. If such a condition be found on two occasions separated by a fortnight's interval, it is not due to the common cold.

TREATMENT

Cure depends only on recognition of the disease. Ephedrine in saline nasal drops is in a great many cases successful. If anterior rhinoscopy shows signs of active disease after a week, ephedrine replacements are given. The age of the child is now no longer regarded as a factor in this decision. My nursing staff will, if asked, give a replacement to any child of any age, usually with, but if necessary without, his co-operation. If still uncured after one month, puncture lavage of the antra rarely fails. In less than 10% of my very severe cases, operation was necessary. When operation is necessary the Caldwell-Luc approach is preferable in children.

The personal factor has not always been co-operative. There have been two authentic cases where dock-labourers working on these cargoes have infested, or transmitted would probably be a better word, the condition to their homes; probably due to carrying infested dust on their clothing. I can only find slight references in the literature to these conditions, and only one or two cases are reported. I have probably seen at least 200 cases of this condition. As I do not treat patients but refer them to their panel doctor, I have had the opportunity of watching numerous varieties of treatment from sulphur ointment to benzyl-benzoate. Calamine lotion seems to give relief and appears to be effective. In all cases there was a desquamation of the skin.

I have submitted various samples to the Zoology Department of the University of Glasgow. Results have been variable and in a copra cargo causing the most trouble clinically, the mites were few and nearly all dead. In one cheese cargo causing a considerable amount of trouble, a temperature of 40° F. was maintained throughout the voyage but the mites nevertheless appear to be more virile in this cheese than in any other cargo. The entomologist who carried out these examinations was Mr. Antony Downes, B.Sc.

Dr. S. A. Henry : It does not come within the province of a Medical Inspector to discuss any decisions on compensation, but I can mention one or two points. The term "dust or liquids" is very broad. Surely in this case there must be dust present, and it is not a question of one mite getting on to the person. The mites travel in dust. The clinical nature of these cases is very interesting. I am not a dermatologist, but I have seen pictures which show distinct bites. With copra itch there is no obvious bite, but there is chemical irritation. It was suggested to me by an entomologist in the course of watching the procedure of a mite on the coconut that it did excrete, changing the matter which it was eating into something else, possibly of a histamine nature, and it was perhaps this chemical getting into the body or on to the skin which caused the irritation, which could be classed as a liquid! The Law does not specify what liquid or what dust.

In some cases there is a distinct bite which might create a different issue, that is, that it was an accidental bite, but if any chemical gets into the skin and causes a rash then it is rather different from a mere bite which may die away in a day or two. I take it that none of these mites burrow into the skin in the same way as the Acarus of scabies. It is not like the lesion of scabies, and, if there is a bite, presumably there will be the insertion of poison.

Dr. Sibyl Horner : I have seen a few cases of copra itch and cheese itch. To deal with cheese itch first—there are perhaps two types. At a factory where cheese was processed, most of the dermatitis seemed to arise from friction with the rind of large cheeses, from which the rind has to be grated by hand. There were a few cases on the mixing side which were thought to be due indirectly to a mite which does not attack the human being but the larvæ are deposited in the cheese where they live on the products of fermentation. This is a matter for the consideration of the medical referee as larvæ might be considered to be dust as might the rind from the cheese although the essential element causing dermatitis is probably friction.

The copra cases are rather interesting because if the irritation was directly due to mite bites one might expect that the subjects would feel the irritation shortly after contact, but apparently they do not, there usually seems to be about twenty-four hours' interval before there is serious complaint of skin irritation, which recalls a chemical dermatitis. In a severe case there is swelling of the eyes, profuse erythema of the neck spreading down the chest, but usually only on the parts of the skin which are exposed to dust. An entomologist has reported the presence in a sample of copra dust of no less than four species of mites, not including either *Pediculoides ventricosus* or *Tyroglyphus longior*, those commonly found in grain and copra itch. A medical referee would have no difficulty, it is suggested, on the question of "dust" in the case of "copra itch".

Other observers have thought that an essential oil in copra dust plays a part and more recently another observer has suggested that inhalation of dust has played some part in the production of an urticarial type of eruption. I think one might distinguish between lesions from bites of mites and those due to irritation from larvæ; the common harvest itch may be an example of the latter group. The adults are said not to actually bite the human host but to deposit the larvæ on the skin while the mites set up a severe skin irritation by their salivary secretion.

cargoes" such as this cheese, or some grain cargoes, will set up such skin irritation that with the added effects of scratching a man may be unable to work for a fortnight. He may quite properly be given a certificate by his panel doctor that he is suffering from dermatitis, to which may or may not be added "Occupational". His Approved Society will then send him to the certifying or examining surgeon to obtain a certificate under the Workmen's Compensation Act.

Should the examining surgeon issue a certificate that this is the disease named in the schedule of the Act, "Dermatitis produced by dust or liquids"? You know that no other "occupational dermatitis" is scheduled. Recently an appeal from a certifying surgeon's certificate of "Dermatitis produced by dust or liquids" came before me. A man had been stripping upholstery from some old buses. It proved to be infested with bugs and the man was incapacitated for some time by recognizable bug bites. I allowed the appeal, for the dermatitis was not produced by dust but by bug bites. This was "an accident arising out of and in the course of the man's employment". But neither the certifying surgeon nor the medical referee is permitted, under the Act, to issue a certificate to this effect. Fortunately the Insurance Company's representative attended at the appeal and was satisfied that the man had been disabled by the bug bites which entitled the workman to compensation for the accident, just as if he had been stung by a scorpion or bitten by a snake, or even, as the Courts have decided, by a malaria-producing mosquito.

Up to the present I have not had to decide an appeal about Tyroglyphus, or Pediculoides bites, but I am inclined to think that if a certifying surgeon issued a certificate of "Dermatitis produced by dust or liquids" in such a case it might be appealed against. It would then be the medical referee's duty to decide whether the condition was in fact the "scheduled disease". At present there are no judicial decisions to guide him, but it may be relevant to point out that the Courts have held that where, in certain circumstances, a workman is disabled by a disease due to an insect-bite, he is entitled to recover compensation as for injury by accident. Applying this to the present case, it would seem that if the mite *Tyroglyphus longior* is not normally found in cheese dust, but that the workman's disability was due to his having worked in the dust on a particular occasion when it happened to be infested, the question of regarding the case as one of injury by accident should not altogether be excluded. If, however, the dermatitis is due to the cumulative effect of exposure to mites in cheese dust over a considerable period, it will not be possible to attribute the workman's condition to a particular accident. In this connexion I may explain that one of the principles governing the scheduling of diseases under the Workmen's Compensation Act is the difficulty of proving that disablement by disease, especially diseases which are contracted gradually or are progressive in character, is of accidental origin. That being so, where incapacity is not accidentally caused, a wide view of the scheduled description of the disease should be taken. The description "dermatitis produced by dust or liquids" does not exclude dermatitis produced by a dust which in itself is not irritating but which harbours insects whose bite does in fact produce dermatitis. There is the further consideration that it may in particular cases be extremely difficult to say with certainty that the cheese-dust itself has not contributed to the condition.

The Workmen's Compensation Act is likely to be amended in the near future and I believe it might be a help to those who will have the task of drafting the amendments if dermatologists could make some suggestions on this point, and perhaps on other aspects of the disease scheduled as "Dermatitis produced by dust or liquids".

REFERENCES

SOLOMON, M. E. (1943) Tyroglyphid Mites in Stored Products : Dept. of Scientific and Industrial Research, H.M. Stationery Office, London.
THOMAS, E. W. PROSSER (1942) *Brit. J. Derm.*, 54, 313.

Dr. Prosser Thomas: Dr. George Buchanan, Medical Officer of the Clyde Navigation Trust, Glasgow, says in a personal communication: During the past two years in the Port of Glasgow we have had numerous outbreaks of cheese itch, linseed itch and copra itch. The cases have varied from very mild to very severe skin eruptions. In addition to the skin eruption, some workmen have shown a neurotic tendency following their recovery. Again, ignorance is playing a great part in retarding their complete recovery. They regard this as a tropical disease, and should scabies occur following recovery, as it has done, the situation becomes even more complicated. For prevention we have tried anti-dermatitis cream, gloves, &c., we have also used the gas cleansing stations in the docks as "Dock Head Baths" in an endeavour to prevent the onset of these itches, without complete success.

days. A day after this test was made, more mites were applied directly under lint and strapping. At the end of three days there was an erythematous patch with pinpoint vesicles.

Since a little of the cheese dust must have still adhered to the mites, these observations could not be held to prove that the irritant was in the saliva, hairs or fæces of the mite.

It has been suggested that it is possible to become immune to the dust containing the Tyroglyphus, and that labourers who have had attacks may lose their sensitivity. Immunity may also be established towards the gastro-intestinal irritant which is present in the cheese in which the *Tyroglyphus longior* is deliberately cultured so that it becomes friable. This cheese is referred to by Hase as "Altenburg" cheese and he gives details of its preparation and states that it has a desirable lemon flavour. Eating undue amounts of the cheese for the first time may produce a gastric disturbance, Hase states, but habitual eaters are immune. The ritual is to tap the cheese to remove excess dust containing mites, before eating.

REFERENCES

DOWLING, G. B., and THOMAS, E. W. PROSSER (1942) *Brit. med. J.* (ii), 543.
FABRE quoted in Louste et Levy-Franckel (1936) *Nouvelle Pratique Dermatologique* (Masson), 2, 57.
HASE, A. (1929) *Z. Parasitenk.*, 1, 765.
PECK, S., and WRIGHT, W. H. (1943) *J. Amer. med. Ass.*, 123, 821.

Dr. S. A. Henry: With regard to the material on which the Tyroglyphus may exist, it is suggested that some chemical is formed from it by the mite. I remember going to an engineering works where some of the girls and men who were working in a storeroom noticed a number of little spots on their necks, with irritation which lasted for a few days. I am not sure whether there were any obvious punctures of the skin, but the Tyroglyphus was discovered in a rat's nest. At first the position was complicated by the discovery of four fleas on the girls' bench, which were found to have emanated from the factory cat, and were not of the human variety. There was nothing on which these mites were known to be feeding, and the question arose as to whether the rash was only caused by the bite of the mite.

We have talked about bites, but what about clawing? Does something enter the skin from the animal, perhaps its own secretion, capable of causing a chemical rash or does it carry on its body some offending dust which comes from cheese, copra, or whatever it may be? The question is whether a rash may develop without chemical change in the cheese or presumably the copra in the same way. There is some evidence that these cases mainly occur spasmodically when the substance in question is particularly old or rotten. They apparently do not occur when good cargoes are handled. The other point is, have we not been taught that certain animals do not like living on certain people, who are therefore immune? I do not know whether the Tyroglyphus is of that type or not. This points to the possibility of a new chemical being formed by the animal and excreted.

The President: I should have thought that most of the evidence supported the idea that some chemical was involved, rather than the actual bites or clawing of the creature, because the worst cases in Glasgow occurred when the mites were dead, and Dr. Forman's experiments showed that an extract of dead mites was as irritating as live ones. The dust, I suppose, consists of mites, larvæ and excreta and possibly some cheese.

Dr. Prosser Thomas, in reply to a question: The "dust" is a fine brown powder coating the surface of the cheese. It may be a quarter of an inch thick and consists of layers of dead bodies of mites, moulted skins, fæces, minute particles of cheese, and the living mites themselves.

The President: It seems to me that it should be compensable. Do you say, Dr. Forman, that the mites definitely do not bite the human being?

Dr. Forman: As far as I know the *Tyroglyphus longior* does not bite. It excretes saliva and then sucks in the softened or dissolved food (Hase).

ADDENDUM (28/4/44): E. W. PROSSER THOMAS, M.D.

Since the above discussion I have carried out patch tests on twenty-five subjects (including myself) with some of the cheese dust brought to me in September 1941 by the first patient I saw with dermatitis due to this cause. This sample is, therefore, more than two and a half years old and is quite inactive on microscopical examination, though there

Dr. G. B. Dowling : There does not appear to be any question of special individual susceptibility to the mites; from the cases that Dr. Prosser Thomas and I saw together, we learned that all those who had handled the offending cheeses were attacked; we noted also that the reaction they provoke is a diffuse erythematous dermatitis without lesions suggesting individual bites. This appears to suggest that some rather powerful chemical irritant may be present in the masses of Tyroglyphus of which the dust is composed; and it would be interesting to know whether masses of dead mites would have the same effect.

The Port Medical Officer at Glasgow said that in the worst outbreak the mites were dead and that fact certainly supports the idea that there may be some chemical irritant in the body of the mites. A further point upon which I think perhaps some stress might be laid is that these cases are not really very serious. The dermatitis clears up rapidly; the cases I have seen have been fit for work in a fortnight.

If exposure continued for a long period a more prolonged type of dermatitis might result, but in those that I have seen it began to clear up in a few days.

Dr. Louis Forman : Cases of acute dermatitis in dockers unloading cheeses reported recently by Dowling and Prosser Thomas suggest that the dust contains an irritant capable of producing a reaction in all contacts. The nature of this irritant, presumably a chemical one, is unknown. There is no evidence that the Tyroglyphidæ bites, but the saliva is said to be able to dissolve keratin, so that I presume it can dissolve the horny layer of the skin. The hairs on the mite's body may be irritant. Fabre is quoted as having demonstrated glands in relation to such hairs (in caterpillars) which he stated to contain an irritant chemical that he isolated. However it was an ethereal extract of a number of caterpillars that was used for the patch test. It is not clear that the glands were isolated and extracted. Then the fæces may contain an irritant. Dr. Prosser Thomas has drawn my attention to an article in which the irritant effect of louse fæces on the skin has been experimentally proved (Peck, Wright and Gant, 1943). Lastly the mite may produce an irritant substance from the fat of the cheese.

Members may remember a case I showed at the British Association of Dermatology and Syphilis Meeting in July 1943, of a storeman with an angry vesicular dermatitis limited to the front of the right wrist. His duties included the moving, cleaning and cutting of cheese, mainly Canadian cheddar. Because of the war these were stored in greater bulk and for a longer time than usual in the Institution in which he worked.

The cheese which I examined was covered with muslin which was damp and largely rotted, and under which was a thick brown layer of dust containing live and dead mites, and eggs.

The man was right-handed, and wore an ordinary coat-type overall. He stripped and scraped the cheese ready for consumption, and was in the habit of rubbing his arm on the front of his coat. It was noted that the eruption took seven weeks to settle down, in contrast to the rapid improvement of the more diffuse erythematous reaction seen in Dowling's cases. Two reasons may be given. Firstly that the reaction was eczematous rather than a simple erythema, and secondly that the dust was still present in his overall and because of this habit of rubbing his wrist on the coat, there was continued contact.

I was informed that two other workers, both women, when handling cheeses in the same store, developed a dermatitis on the wrists and arms.

The following patch tests were made on this patient: (1) Cheese dust was applied under moist lint and allowed to remain on for forty-eight hours with a strong vesicular result. (2) Cheese dust was extracted with ether, spirit and with saline, and the supernatant liquid in each case was applied on lint. The spirit and ether extracts gave a positive result after twelve hours, but the saline extract gave no reaction. All this tells us is, that the irritant is probably ether and spirit soluble.

I applied the dust under damp lint to my forearm for forty-eight hours with a negative result. After a week, the dust was applied again and a patch of acute vesicular dermatitis developed which took two weeks to subside. Thus a sensitization promptly occurred.

Mr. Browning of the British Museum made a culture of the mites, growing them on cheese in a damp atmosphere. He sent me some of the mites which I then applied to my forearm under a glass capsule so that the reaction could be observed. This was applied at the site of the positive patch carried out ten weeks previously. After twenty-four hours no movement of the mites could be seen. At the end of forty-eight hours minute papules appeared under the mites and the papules became more definite after four

the neck. I ordered marmite in the first place and later tried the effect of nicotinic acid, feeling that the eruption was pellagroid in nature, and when I saw her again to-day she stated that there was a considerable improvement.

Dr. Hugh Stannus: Various skin conditions may respond to nicotinic acid apart from pellagra, possibly due to its pharmacological action. In this particular case, I think, a deficiency of riboflavin might be considered in view of the mild erythematous rash on the face, and the affection of the ears and lips. This woman has moreover an affection of the angles of the mouth. She is certainly not typical of riboflavin deficiency but, on the other hand, there are odd cases which do react to riboflavin.

Pustular Bacteride with Acute Relapse following Sore Throat in a Patient with Psoriasis of the Scalp.—Louis Forman, M.D.

Typical grouped pustules and vesicles on the feet, particularly the left instep.

History of scaly areas in the scalp present for two and a half years, clinically psoriasis. (This was observed subsequent to the case being shown.)

Fourteen days ago developed sore throat and catarrh. Ten days ago numerous small pin-head-sized papules, some pustular, on legs and thighs, with vesicles and pustules on the palms.

Some of the small pustules had dried and scaled within a few days. The pustules on the feet were sterile on culture.

Dr. Dowling: I find great difficulty in these cases in discovering any suggestive focus with which one can deal. I should be glad to be convinced that they were all due to some focus of infection.

I had charge of a patient who, having had an attack of quinsy, had her tonsils removed. The pustular eruption on the soles cleared up immediately afterwards.

The President: I can remember one case in a surgeon who had extraordinarily resistant pustules on both hands. Nothing did him any good until he had his tonsils out and after that the hands cleared up and he has had no recurrence.

? Lichen Sclerosus et Atrophicus.—Geoffrey Duckworth, M.R.C.P.

Mrs. W., aged 65.

For nearly three years has complained of a non-itchy eruption on the backs of the hands, forearms, and neck. On the back of the hands there are whitish, flat-topped, angular papules, and these extend on to the backs and fronts of the wrists. On the forearms the lesions, which were whitish when first seen, about a fortnight ago, are now purplish red macules, some of which have an atrophic appearance. Definite atrophy is to be seen about the wrists. On the back and sides of the neck there are whitish papules, and on the exposed "V", over the upper part of the sternum, there is a conglomeration of the purplish-red macules.

The buccal mucosa is clear, but there is a suggestion of reticulated whitish stippling on the upper gums, seen when the denture is removed. Elsewhere there is some rosacea of the face; the tongue is rather more furrowed than usual; and there is indigestion of the ? nervous type. She has been treated with tablets containing nicotinic acid, riboflavin, and aneurine, internally, and an emulsifiable cream containing 2% each of salicylic acid and liq. carb. detergens, externally.

The President: It is not quite my idea of lichen sclerosus. The lesions seem to be follicular. I do not know what to call it.

Dr. G. B. Dowling: I have seen this condition on several occasions in people getting on in years, in front of the forearm and wrists and sometimes in front of the ankles, dorsum of the feet, and legs. I have no idea of its cause or correct classification.

One such case was reported on by C. D. Freeman. *Archives of Dermatology and Syphilis* (1926), 13, 489, under the title "Erythematous Lichen Planus". Dr. Freeman held that his case corresponded to Radcliffe Crocker's description of erythematous lichen planus, with which view I do not personally agree, though it may be one of the numerous clinical varieties of lichen planus. There are two photographs in the report.

The President: In this case it was on the areas exposed to the sun, and I thought it might have something to do with atrophy, the result of long exposure to light.

Lupoid (Boeck's Sarcoid).—I. R. Marre, M.R.C.S., L.R.C.P.

Mrs. M. A., aged 34. She first noticed a blue patch on left big toe over three years ago, followed by a patch on the second left toe and then two patches on the outer border of left foot. Two years ago she noticed a large bluish patch on left cheek, followed by

are still numbers of undisintegrated bodies of mites to be seen. The mite in this specimen had been identified by Mr. E. Browning, Department of Zoology, British Museum (Natural History), as *Tyroglyphus longior* var. *Castellanii*, Hirst, the mite that causes itch in handlers of copra. As Dowling stated in the discussion, the dermatitis observed in this patient and in others handling the particular cheeses was of the diffuse erythematous contact type without any clinical evidence of individual bites.

I applied some of this dust either to the forearm or the interscapular area under a square of plain white lint, which was fixed in position in the usual way with a larger square of adhesive tape. I examined the areas in forty-eight or seventy-two hours. The results were as follows: Strongly positive, 7 cases (raised erythema with papules and vesicles); positive, 3 cases (raised erythema only); negative, 15 cases. In one case the reaction was so strong as to result in a small superficial ulcer which took about ten days to heal.

Erythematous Lichen Planus —G. B. DOWLING, M.D.

F. C., female, aged 37, Clerk.

This patient presented herself at St. Thomas's Hospital in January 1943 with a lichen planus presenting unusual features, especially a deep red erythema occupying the whole of the face, and extending over the mandible on to the neck. This had been present for six years, or longer. It had been preceded for some years by a bald scarred area in the scalp. In addition to these two lesions she had red horny lesions on the fingers and hands which might be difficult to distinguish from the chilblain type of lupus erythematosus; a small erosion on the vulva, and a few small papules of the ordinary lichen planus type on the forearms. With regard to the erythema of the face, this is slightly rough to touch, but has never presented the scaling characteristic of lupus erythematosus, or any follicular plugging. The scarred area in the scalp has about it some spiny lesions of the lichen pilaris type. On each side of the buccal mucous membrane there is the whitish reticulation characteristic of lichen planus but with rather more inflammatory redness than is usual in the mouth. Along the vermilion of the lower lip there is a bluish streak, superficial, horny, and showing the whitish reticulation characteristic of lichen planus (Wickham's striæ). The diagnosis is lichen planus showing unusual features.

The President: This is certainly a case of lichen planus though as a rule it does not occur on the face. I do not remember seeing a case with so much lichen planus on the face except for one other case which was that of a woman with an annular lichen planus on the forehead.

Major Hellier: I would like to report two cases of lichen planus in men from overseas of a type I have never seen before. I had not seen a case on the face until just recently when I went to a hospital and saw a case under the care of Major Barker, of confluent warty lichen over the whole of the legs and thighs with lesions on the neck, the ears, round the eyes, on the insides of the cheeks and the lips. I had never seen a case like that before yet in the next bed was a man with the same picture—the same legs, the same "spectacles" round the eyes, and the same extensive lesions in the mouth. Incidentally, neither of these men had genital lesions.

Both men had come back from overseas, one from West Africa and the other from North Africa. We discussed the possible causes and considered whether it was the result of exposure to sunlight or whether it could have been due to lack of vitamin B. Major Barker was very much in favour of the latter. Both cases improved when put on vitamin B in the form of food yeast.

I would not accept lack of vitamin B as being the cause without reserve. The men had been overseas with all the worry and danger attached, they had come home to this country, and had been put into a comfortable hospital, their minds were relieved and there was a very good reason for the lichen planus to clear up. It is possible, however, that the lesions inside the mouth and on the face were due in part to vitamin B lack.

The President: For two or three years I have treated all my cases of lichen planus in the first place with vitamin B_1, some respond and clear up in a most dramatic manner. There was a soldier from Libya in the Masonic Hospital who had a severe attack; he had been in hospital in London for two or three weeks and had not improved at all. Then we put him on about 9 mg. of vitamin B_1 daily and he improved in the most astonishing manner. I remember a number of cases which improved in this way, but others are not affected at all.

I do not suggest that lichen planus is due to a vitamin deficiency. I suppose the aneurin acts pharmacologically.

Dr. I. Muende: I saw a similar case some six weeks ago where the patient, a young woman, had an extensive erythema of her face, with lichenoid papules at the margin of the normal skin beyond, with similar papules over the manubrium sterni and nape of

more inches in diameter. The most notable are: one at the side of the nose, and those on the right elbow, back, and left thigh. There are some small ones about the feet and legs.

On general examination no abnormality was found, but the patient suffers from arthritis of the right wrist and the ankles, for which X-ray treatment has been given with considerable benefit. No abnormality was found on X-ray examination of the joints, but the proximal phalanges are said to show changes suggestive of sarcoidosis. X-rays of chest revealed nothing abnormal. The urine was normal. The blood-count showed slight relative lymphocytosis. The blood uric acid was 6·1. The Wassermann was negative, and the Mantoux test positive at 1:1,000 and 1:10,000 mg. Treatment with arsphenamine, mercury, and potassium iodide had no effect. In the last few weeks he has been on liquor arsenicalis, and during this time there has been obvious flattening of the lesions.

The section was described by the pathologist as "typical of sarcoid of Boeck".

The President: Clinically this is a typical sarcoid, but the Mantoux is positive, and in sarcoid there is not supposed to be a positive Mantoux until the final tuberculous illness has developed.

Dr. Robert Klaber: It is unusual to get a strongly positive Mantoux in a case of this type. I am told it was positive with 1:10,000 as well as to a 1:1,000 dilution. Another slightly unusual feature is the relatively large number of giant cells present in some parts of the section though, again, that is not incompatible with the clinical diagnosis of sarcoid. This man, however, has been about, all over the world, and it seems worth while at least bearing in mind the possibility of the sarcoid form of leprosy.

Lieut.-Colonel F. F. Hellier: Sulzberger in his recent work (Dermatologic Allergy, M. B. Sulzberger, 1940, Springfield) on dermatological allergy stresses that the Mantoux test must be considered as a curve and not an individual reading. In a series of cases of frank tuberculosis, there will be a peak at 1:10,000 or 1:100,000, but even then an occasional case may have a negative Mantoux at 1:100. In Boeck's sarcoid, on the other hand, there is a peak in the lower dilutions, but there may be an odd case positive at 1:100,000. We must not overstress the importance of a single Mantoux test as a diagnostic entity, its significance lies in the spread over a series of cases.

Dr. H. C. Semon: I can remember a case in which we failed to find the leprosy bacillus at the first examination and a year later we did find it. In that case there was a single plaque, very similar to the one shown to-day, at the back of the neck, which at one time I thought might be a sarcoid. The patient had come from the Malay States, and in view of that, I thought it probable that she would eventually become a case of frank leprosy, which she did. I think that another biopsy ought to be done in Dr. Corsi's case. The nasal secretion might also be examined.

Dr. Corsi: The number of cases of sarcoid shown in this section, in which the diagnosis was certain or almost certain, were four only in the ten years 1933-42. In two the Mantoux test was positive, one case shown by Dr. Klaber and the other by Dr. Forman. It would not seem therefore that one should allow oneself to be too much influenced in the diagnosis of sarcoid by the result of a Mantoux test.

The possibility of the case shown to-day being one of leprosy is suggested by the fact that the man has been in many tropical countries. That sarcoidosis is an attenuated form of leprosy is a theory which is discussed by Kissmeyer (La Maladie de Boeck, Paris, 1932). He discusses the theory, and the evidence supporting it, to refute it, as he does the evidence that a sarcoid is an attenuated form of tuberculosis. He concludes that sarcoidosis of Boeck is a disease *sui generis*.

It seems difficult to make the case shown to-day into a case of leprosy, whereas, if such a thing as sarcoidosis exists, the case will fit that diagnosis as well as almost any other case that has been shown to this Section.

Two Cases of Lichen Planus.—G. B. Dowling, M.D.

CASE I.—E. G., female, aged 63. She first noticed a spot behind the right ear five years ago, followed by a similar one behind the left ear. They then gradually began to appear in the scalp, she says, in the form of little pimples, followed by loss of hair. More recently (that is within the last six months or so) she has developed spots on the back of the neck and on the upper part of the back and chest.

She exhibits a large number of bald patches of the pseudopelade type throughout the scalp. They are discoid, confluent in places, leaving the usual islands of normal skin from which hair is growing. On the neck, chest and upper part of the back there is a scattered eruption of the typical lichen plano-pilaris type. Some of these spots have been found in the axillæ, but so far there has been no loss of hair there. The pubic hair has almost disappeared, but there is no obvious scarring. On the buccal mucous membranes on each side she has the characteristic milky-white reticulation of

a patch on the right third toe and outer border of right foot. Finally a year ago a blue granulomatous swelling appeared on the right side of nose. At present there are blue granulomatous patches in all the above situations, showing faint stippling on diascopy. Her tonsils appear normal and there is no enlargement of lymph glands or spleen. Her family and personal history are completely normal.

Investigations.—(1) Mantoux (1:100, 1:1,000, 1:10,000) all completely negative. (2) Wassermann reaction negative. (3) Blood-count within normal limits. (4) Histological section shows typical superficial Boeck type sarcoid (Ziehl-Neelsen stain showed no acid-fast bacilli). (5) Radiological examination showed no changes in the chest, hands, feet, or nasal bones.

Treatment.—(1) Weekly deep subcutaneous injections of sodium morrhuate for two months—no effect. (2) X-ray therapy (250 r) on several foot patches—no effect. (3) A total of 1 g. myocrysin over ten weeks—no effect. (4) Weekly injections of bismuth salicylate intramuscularly for three months—no effect.

The President: This seems to be a typical case of sarcoid or lupoid.

Dr. F. Parkes Weber: I think the case is one of those included under the general term "sarcoidosis"—a term now used, especially by writers on internal medicine all over the world. In fact, the condition of the nose is a one-sided example of Hutchinson's "lupus pernio", which is now considered to be the most characteristic form of Boeck's sarcoid.

Dr. Marre: Goldsmith classed them under lupoids, they are known as lupoids in Macleod and Muende's "Pathology of the Skin", and in America they tend to class them under lupoids. Dr. Parkes Weber says it is like lupus—then why not lupoid?

The President: Personally I think it is better to stick to the original term "sarcoid" as this is the name best known and generally used. I do not know whether you have tried arsenic by the mouth. I remember a case like this where no injections were of any use but when we gave liquor arsenicalis by the mouth the lesions cleared up.

? Leiomyoma. ? Fibrocellular nævus.—BERNARD GREEN, M.R.C.S., L.R.C.P.

Girl, aged 12 years.

This child had an abrasion of the forehead at the age of 2 years. At the age of 3 a few hard nodules appeared on the left temple and each year a few more appeared. These are sometimes painful. Now there is considerable disfigurement with a group of hard elevated discrete nodules, about the size of a pea, on the left temple and forehead. They are of a brownish colour and movable with the skin.

A biopsy was made and the section reported on as leiomyoma. Another authority disagreed and reported the section as a fibrocellular nævus.

Two sections were shown, one stained by the van Gieson method.

Dr. Freudenthal: The section shows mainly fibromatous tissue. It might be worth while making further histological examinations.

The President: Is it not an unusual situation for a leiomyoma?

Dr. Freudenthal: They have been found on practically any part of the body including the face.

Dr. Dowling: I am under the impression that all the cases I have seen were red; this is brownish, almost like a mole in places.

The President: All those which I have seen have been more red with a curious kind of translucence about them. Were the lesions pigmented?

Dr. Green: They were slightly brownish and apparently a few nodules appear each year.

The President: So that she is getting more all the time. Has any member any suggestions for dealing with it?

Dr. Dowling: You would be more likely to do more harm than good by trying to deal with them unless it was by complete excision and graft.

[*March 16, 1944*]

Sarcoidosis.—H. CORSI, F.R.C.S.

Male, aged 64. In the autumn of 1943 patches of redness appeared in various parts of the body, soon followed by lumps. There have never been any symptoms.

Examination in February 1944 showed thick plaques of infiltration with erythema beneath an apparently normal, or nearly normal, epidermis. There is a tendency for the larger plaques to become circinate, and a centrifugal march has been observed in these during the last three or four months. The lumps are of all sizes up to 2 or

more inches in diameter. The most notable are: one at the side of the nose, and those on the right elbow, back, and left thigh. There are some small ones about the feet and legs.

On general examination no abnormality was found, but the patient suffers from arthritis of the right wrist and the ankles, for which X-ray treatment has been given with considerable benefit. No abnormality was found on X-ray examination of the joints, but the proximal phalanges are said to show changes suggestive of sarcoidosis. X-rays of chest revealed nothing abnormal. The urine was normal. The blood-count showed slight relative lymphocytosis. The blood uric acid was 6·1. The Wassermann was negative, and the Mantoux test positive at 1:1,000 and 1:10,000 mg. Treatment with arsphenamine, mercury, and potassium iodide had no effect. In the last few weeks he has been on liquor arsenicalis, and during this time there has been obvious flattening of the lesions.

The section was described by the pathologist as "typical of sarcoid of Boeck".

The President: Clinically this is a typical sarcoid, but the Mantoux is positive, and in sarcoid there is not supposed to be a positive Mantoux until the final tuberculous illness has developed.

Dr. Robert Klaber: It is unusual to get a strongly positive Mantoux in a case of this type. I am told it was positive with 1:10,000 as well as to a 1:1,000 dilution. Another slightly unusual feature is the relatively large number of giant cells present in some parts of the section though, again, that is not incompatible with the clinical diagnosis of sarcoid. This man, however, has been about, all over the world, and it seems worth while at least bearing in mind the possibility of the sarcoid form of leprosy.

Lieut.-Colonel F. F. Hellier: Sulzberger in his recent work (Dermatologic Allergy, M. B. Sulzberger, 1940, Springfield) on dermatological allergy stresses that the Mantoux test must be considered as a curve and not an individual reading. In a series of cases of frank tuberculosis, there will be a peak at 1:10,000 or 1:100,000, but even then an occasional case may have a negative Mantoux at 1:100. In Boeck's sarcoid, on the other hand, there is a peak in the lower dilutions, but there may be an odd case positive at 1:100,000. We must not overstress the importance of a single Mantoux test as a diagnostic entity, its significance lies in the spread over a series of cases.

Dr. H. C. Semon: I can remember a case in which we failed to find the leprosy bacillus at the first examination and a year later we did find it. In that case there was a single plaque, very similar to the one shown to-day, at the back of the neck, which at one time I thought might be a sarcoid. The patient had come from the Malay States, and in view of that, I thought it probable that she would eventually become a case of frank leprosy, which she did. I think that another biopsy ought to be done in Dr. Corsi's case. The nasal secretion might also be examined.

Dr. Corsi: The number of cases of sarcoid shown in this section, in which the diagnosis was certain or almost certain, were four only in the ten years 1933-42. In two the Mantoux test was positive, one case shown by Dr. Klaber and the other by Dr. Forman. It would not seem therefore that one should allow oneself to be too much influenced in the diagnosis of sarcoid by the result of a Mantoux test.

The possibility of the case shown to-day being one of leprosy is suggested by the fact that the man has been in many tropical countries. That sarcoidosis is an attenuated form of leprosy is a theory which is discussed by Kissmeyer (La Maladie de Boeck, Paris, 1932). He discusses the theory, and the evidence supporting it, to refute it, as he does the evidence that a sarcoid is an attenuated form of tuberculosis. He concludes that sarcoidosis of Boeck is a disease *sui generis*.

It seems difficult to make the case shown to-day into a case of leprosy, whereas, if such a thing as sarcoidosis exists, the case will fit that diagnosis as well as almost any other case that has been shown to this Section.

Two Cases of Lichen Planus.—G. B. DOWLING, M.D.

CASE I.—E. G., female, aged 63. She first noticed a spot behind the right ear five years ago, followed by a similar one behind the left ear. They then gradually began to appear in the scalp, she says, in the form of little pimples, followed by loss of hair. More recently (that is within the last six months or so) she has developed spots on the back of the neck and on the upper part of the back and chest.

She exhibits a large number of bald patches of the pseudopelade type throughout the scalp. They are discoid, confluent in places, leaving the usual islands of normal skin from which hair is growing. On the neck, chest and upper part of the back there is a scattered eruption of the typical lichen plano-pilaris type. Some of these spots have been found in the axillæ, but so far there has been no loss of hair there. The pubic hair has almost disappeared, but there is no obvious scarring. On the buccal mucous membranes on each side she has the characteristic milky-white reticulation of

more inches in diameter. The most notable are: one at the side of the nose, and those on the right elbow, back, and left thigh. There are some small ones about the feet and legs.

On general examination no abnormality was found, but the patient suffers from arthritis of the right wrist and the ankles, for which X-ray treatment has been given with considerable benefit. No abnormality was found on X-ray examination of the joints, but the proximal phalanges are said to show changes suggestive of sarcoidosis. X-rays of chest revealed nothing abnormal. The urine was normal. The blood-count showed slight relative lymphocytosis. The blood uric acid was 6·1. The Wassermann was negative, and the Mantoux test positive at 1:1,000 and 1:10,000 mg. Treatment with arsphenamine, mercury, and potassium iodide had no effect. In the last few weeks he has been on liquor arsenicalis, and during this time there has been obvious flattening of the lesions.

The section was described by the pathologist as "typical of sarcoid of Boeck".

The President: Clinically this is a typical sarcoid, but the Mantoux is positive, and in sarcoid there is not supposed to be a positive Mantoux until the final tuberculous illness has developed.

Dr. Robert Klaber: It is unusual to get a strongly positive Mantoux in a case of this type. I am told it was positive with 1:10,000 as well as to a 1:1,000 dilution. Another slightly unusual feature is the relatively large number of giant cells present in some parts of the section though, again, that is not incompatible with the clinical diagnosis of sarcoid. This man, however, has been about, all over the world, and it seems worth while at least bearing in mind the possibility of the sarcoid form of leprosy.

Lieut.-Colonel F. F. Hellier: Sulzberger in his recent work (Dermatologic Allergy, M. B. Sulzberger, 1940, Springfield) on dermatological allergy stresses that the Mantoux test must be considered as a curve and not an individual reading. In a series of cases of frank tuberculosis, there will be a peak at 1:10,000 or 1:100,000, but even then an occasional case may have a negative Mantoux at 1:100. In Boeck's sarcoid, on the other hand, there is a peak in the lower dilutions, but there may be an odd case positive at 1:100,000. We must not overstress the importance of a single Mantoux test as a diagnostic entity, its significance lies in the spread over a series of cases.

Dr. H. C. Semon: I can remember a case in which we failed to find the leprosy bacillus at the first examination and a year later we did find it. In that case there was a single plaque, very similar to the one shown to-day, at the back of the neck, which at one time I thought might be a sarcoid. The patient had come from the Malay States, and in view of that, I thought it probable that she would eventually become a case of frank leprosy, which she did. I think that another biopsy ought to be done in Dr. Corsi's case. The nasal secretion might also be examined.

Dr. Corsi: The number of cases of sarcoid shown in this section, in which the diagnosis was certain or almost certain, were four only in the ten years 1933-42. In two the Mantoux test was positive, one case shown by Dr. Klaber and the other by Dr. Forman. It would not seem therefore that one should allow oneself to be too much influenced in the diagnosis of sarcoid by the result of a Mantoux test.

The possibility of the case shown to-day being one of leprosy is suggested by the fact that the man has been in many tropical countries. That sarcoidosis is an attenuated form of leprosy is a theory which is discussed by Kissmeyer (La Maladie de Boeck, Paris, 1932). He discusses the theory, and the evidence supporting it, to refute it, as he does the evidence that a sarcoid is an attenuated form of tuberculosis. He concludes that sarcoidosis of Boeck is a disease *sui generis*.

It seems difficult to make the case shown to-day into a case of leprosy, whereas, if such a thing as sarcoidosis exists, the case will fit that diagnosis as well as almost any other case that has been shown to this Section.

Two Cases of Lichen Planus.—G. B. DOWLING, M.D.

CASE I.—E. G., female, aged 63. She first noticed a spot behind the right ear five years ago, followed by a similar one behind the left ear. They then gradually began to appear in the scalp, she says, in the form of little pimples, followed by loss of hair. More recently (that is within the last six months or so) she has developed spots on the back of the neck and on the upper part of the back and chest.

She exhibits a large number of bald patches of the pseudopelade type throughout the scalp. They are discoid, confluent in places, leaving the usual islands of normal skin from which hair is growing. On the neck, chest and upper part of the back there is a scattered eruption of the typical lichen plano-pilaris type. Some of these spots have been found in the axillæ, but so far there has been no loss of hair there. The pubic hair has almost disappeared, but there is no obvious scarring. On the buccal mucous membranes on each side she has the characteristic milky-white reticulation of

lichen planus. A point of interest is that it could not have been possible to identify this case with lichen planus until fairly recently, there being nothing in the old and very progressive scalp lesions to distinguish the condition from pseudopelade.

The President: I do not remember seeing such a dramatic case for a long time.

Dr. H. C. Semon: Is it the general experience that when lichen planus attacks the scalp a permanent baldness develops in situ? I do not know why lichen planus should cause atrophy to that extent.

The President: It does not very often attack the scalp.

Dr. Semon: I quite agree. I have never seen a case in my own practice.

Dr. Dowling: I have seen lichen planus in the scalp on more than one occasion. It might be like this case or it might resemble lichen simplex.

The President: This patient said that the condition started with pustules behind the ears, but of course, patients' descriptions are vague. There is no evidence of pustules now.

CASE II.—F. N. L., male, aged 51. In March 1943, while on the Gold Coast, he became aware of two spots just inside the corners of the lips which felt rough and dry. This was followed by swelling in the right foot. At the time he attended the out-patient department of the hospital at Accra, during which period an extensive eruption began to develop, chiefly on the limbs. Eventually he became dangerously ill with high fever and was unconscious for some weeks.

He recovered gradually, and by December was physically quite fit, but the eruption was no better.

He presents a very extensive lichen planus of the hypertrophic type affecting chiefly the neck, arms, legs and thighs. The lichen planus is deeply pigmented, and this contrasts with neighbouring areas of depigmentation. A few characteristic papules are to be found on the scrotum, and a little on the buccal mucous membrane on the left side. It appears that he was regarded in West Africa as a mixed type of vitamin deficiency, the clinical picture being one of mixed pellagra and beri-beri. The diet consisted of meat, eggs, rice, plenty of fruit, but there were no green vegetables, no butter, and no potatoes. He was treated with cod-liver oil, nicotinic acid and riboflavin.

I have brought the case up for two reasons: (1) To have the diagnosis confirmed for the sake of the records, and (2) because he is exactly like another case of very extensive hypertrophic lichen planus with marked pigmentation that I saw recently in a soldier returned from Africa. Major Hellier at the last meeting of the Section referred to two similar cases, also from Africa. The patient is at present being treated with vitamin B_1 9 mg. daily, and nicotinamide.

(This case was referred to me last month by Dr. Brunel Hawes of the Colonial Office.)

Major Twiston Davies: A case of this kind from West Africa had the most extensive lichen planus I have ever seen. The man's lower extremities resembled trunks of trees, and he had on his face a formation of lichen planus which made him appear to be wearing horn-rimmed spectacles. We kept him in bed, and gave him liquor arsenicalis by the mouth until he complained of it, and after that liquor hydrarg. perchlor. He did extremely well, and little now remains of the disease save pigmentation.

Lieut.-Colonel F. F. Hellier: One of the cases about which I spoke at the last meeting is now under Major Twiston Davies. Not only was there one man with this condition, but in the next bed another man with the same picture: the same tree trunk limbs, the same spectacle-like lesions on the face. A minor point was that in each the penis was quite clear as it is in the case presented to-day. The lesions inside the mouth, I gather, cleared up before the case reached Major Twiston Davies, and the mucous membrane of the lip cleared very rapidly. One of these men was from North Africa, the other two—for there were three in all—from West Africa.

Vitamin deficiency may have been a causal factor and some people are more sensitive to such a deficiency than others. This may have combined with a lichen planus tendency to produce this peculiar picture.

Brigadier R. M. B. MacKenna: Recently a senior officer, aged 57, was invalided from West Africa, suffering from very severe generalized lichen planus, but not of the hypertrophic type nor particularly pigmented. The one reason why this might possibly link up with Dr. Dowling's case is that when this officer was in a transport on his way from this country to West Africa he developed an acute pyrexia of unknown origin and was very ill. The fever, which was accompanied by fairly severe mental aberration, subsided after fourteen days; a month later, for no apparent reason, severe lichen planus appeared. Eventually he returned to England and passed into Major Mannix's care; he was treated with X-rays applied to the lesions and not to the spine, and by mercury internally. He made excellent progress.

Darier's Disease.—E. W. PROSSER THOMAS, M.D.

Mrs. A. H., aged 62, has had Darier's disease for fifty years. There is no family history of skin disease. The eruption is extensive and of the classical distribution and character. On the soles, in addition to a number of yellowish punctate keratoses, there is a profusion of warty excrescences, and the horny filiform tufts at the ends of the toes and along the toe margins are also very striking. One might also be impressed by the effect one gets of a systematized nævus, particularly on the front of the trunk, where the eruption is divided down the mid-line by a narrow clear zone. A rather unusual feature in the case seems to be the absence of a pigmented background.

Dr. I. Muende : Might not the reason for the relatively small amount of pigmentation be that the patient is a blonde? Most cases of Darier's disease are brunettes and the pigmentation is due to an over-activity of the epidermis which, of course, would be much less marked in a fair-skinned patient.

The President: She is definitely less brown than these cases mostly are. Has any member any experience of trying a high dose of vitamin A in Darier's disease?

Dr. A. D. Porter: We had a male patient to whom 100,000 units of vitamin A a day were given for about four months, and he responded extremely well, but the skin never became quite normal. A woman who has suffered from his condition all her life gained considerable benefit from taking 100,000 units daily for about two months, though the improvement was far less than in the first case.

In a third case in a woman also, who took 100,000 units daily for about six weeks, there was no apparent benefit at all. She described the eruption as "Coming and going with the leaves"; appearing in spring and disappearing in the autumn.

Dr. Prosser Thomas : Some time ago I treated a case of Darier's disease of mild degree in a girl with vitamin A, at least 100,000 units a day for some months. without obvious improvement.

Dr. Robert Klaber: Dr. Alice Carleton in a recent paper (*Arch. Derm. Syph.*, 1943, 48, 143) reported four cases of Darier's disease in none of which any evidence of vitamin A deficiency was found, but two out of the four responded dramatically to vitamin treatment, though in the other two cases it apparently had no effect.

The President: It was presumably a purely pharmacological action of the vitamin.

Dr. Klaber : At least it was empirical.

Epithelioma Adenoides Cysticum (Nævus Follicularis of Brooke).—C. H. WHITTLE, M.D.

Married woman, aged 31. There was a history of gradual appearance, starting in late adolescence, of small pale papules on the forehead, cheeks, and chin. These became more noticeable after the birth of her first child. There is no suggestion of other abnormality, endocrine or metabolic. The family history yields no evidence of any other members being similarly affected.

The lesions, which are numerous, are confined to the face, and consist of pale yellowish rounded papules, the smaller ones resembling milia, but varying in size up to 3 or 4 mm. in diameter. The largest are situated on the skin of the upper lip near the nasolabial fold, and they are grouped most thickly in this region, on the inner parts of the cheeks, on the chin, and fairly thickly over the forehead, affecting therefore chiefly the central part of the face. The nose itself is fairly clear. The scalp and skin of the face show a moderate degree of the oily type of seborrhœa. The hair is dark brown, almost black.

The biopsy report of a small lesion taken from the temporal region is as follows: "The tumour appears to be chiefly due to cystic distension of the upper part of a follicle with pink staining horny matter, more or less laminated. There are also to either side fairly superficially placed masses of cells of basal type, arranged in fairly regular palisade form so as to suggest an attempt at formation of a hair follicle. Irregular masses of elastic tissue are to be seen just beneath the epidermis, and this layer is somewhat uneven and broken up; there is slight perivascular infiltration.

"There is no sign of malignant change and the picture accords well with an early stage of Brooke's follicular nævus."

Dr. Whittle showed two sections: the first, taken from this patient demonstrated the early epithelial hyperplasia occurring in the zone around the gross follicular plugging: the second, taken from a single lesion 1½ in. in diameter on the leg of a soldier. The latter, shown by the courtesy of Dr. R. Williamson, illustrated the diversity of conditions classified by pathologists, as opposed to dermatologists, under the term epithelioma adenoides cysticum (e.g. Ewing, 1940).

Brigadier R. M. B. MacKenna: This is a typical case of epithelioma adenoides cysticum. Some years ago, at a meeting of the North of England Dermatological Society at Manchester it was said that in deciding on purely clinical grounds whether the case was one of epithelioma adenoides cysticum or the fleshy type of adenoma sebaceum, it was advisable to inspect the upper lip. Usually this is severely affected in the former condition and either unaffected or sparsely affected in the latter.

Dr. Whittle: Follow-up of these cases shows that a number do go on to malignancy (e.g. Savatard, 1938). Sutton (1939) states that practically all basal-celled carcinomata arise from lesions which are indistinguishable from epithelioma adenoides cysticum.

REFERENCES

EWING, J. (1940) Neoplastic Diseases, 4th Edition, pp. 371, 905 *et seq.* Philadelphia and London.
SAVATARD, L. (1938) *Brit. J. Derm.,* 50, 333.
SUTTON, R. L., and SUTTON, R. L., Jnr. (1939) Diseases of the Skin, 10th Edition, p. 675. London.

Fragilitas Crinium (? Trichorrhexis Nodosa).—C. H. Whittle, M.D.

Male, aged 30. Occupation radio mechanic. There is six months' history of breaking of hair in patches, which are increasing in extent. He knows no cause for this. There are now several patches of 2 in. or more in diameter in which the hairs are broken off to $\frac{1}{2}$ in. or so long, and the hair on these patches appears dry and rather lustreless. On his first visit there was slight reddening and thickening of some of the follicles on the patches suggesting an inflammatory cause. Scales and hairs do not fluoresce under Woods's glass, nor do they show fungus in potash preparations. He appears well in other respects, but has some carious dental stumps.

The hairs break readily on bending, and the ends often show the "paintbrush" appearance, but typical nodes are not found nor is there any noticeable splitting of the hair. Many of the larger hairs show lack of uniform thickness and pigmentation throughout their length, being thicker towards the root, tapering gradually to about half the diameter at a distance of $\frac{3}{4}$ in. from the root, and then widening out again towards the broken end. The root is often deformed, atrophied, or bent on itself at an acute angle. The medulla is frequently absent. Some of the hairs appear to be elliptical instead of circular in cross section. There is no twisting noted. Many of the features mentioned have been reported in trichorrhexis nodosa, but the nodose character is missing.

The President: Was it possibly a case of trichotillomania? I asked the patient if it irritated, but he would not admit that.

Dr. Whittle: "Paint-brush" ends are not peculiar to trichorrhexis nodosa. I have seen it in ringworm infected hairs. But would rubbing the part produce fragility? I should like to inquire further before accepting the President's suggestion.

Dr. Dowling: There can be trichorrhexis nodosa in one area of the scalp and not in another. This, however, looked to me extraordinarily like a case of hair-pulling. It is seen in children as a rule, but I have seen it in adults. I recall it in one case of a youth who derived the habit from his father. His father was an author and in the throes of composition was accustomed to twist and pull his hair.

Postscript (4.4.44).—I have made careful inquiry both at his home and at his place of work. No pulling or rubbing has ever been noticed. Moreover, multiple *nodes* have been found in a few of several hairs since examined. I think trichorrhexis nodosa is the more likely diagnosis.—C. H. W.

Section· of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

[*January* 21, 1944]

Placental Circulation

By NINIAN McI. FALKINER, M.D., F.R.C.O.G.

Master, Rotunda Hospital, Dublin

THE human placenta according to Grosser is described as a placenta hæmochorialis, thereby meaning that the fœtal chorion is in direct relationship with the maternal blood.

This fact underlies many of the risks that the pregnant, parturient and puerperal woman undergoes and it follows that a sound knowledge of the vascular conditions in the pregnant uterus underlies the pathology of reproduction. For instance: do we really understand the mechanism of antepartum and postpartum hæmorrhage or the factors that are associated with embolus complicating childbirth? Advancement in obstetrics depends to some extent on the complete knowledge of this subject.

Spanner's work, published in 1935, depended on very exhaustive and patient injection experiments on the pregnant uterus and placenta, the results of which allowed him to formulate a new idea not only of the structure of the placenta but of the circulation of the maternal blood through that organ and back to the uterine veins.

I will first attempt to describe Spanner's conception of the human placenta in situ.

Fig. 1.—This is a reproduction from Spanner's monograph and shows the main points with regard to his theories of placental structure and circulation. A photographic reproduction of this figure does not do it full justice and the reader may be referred to the original monograph for a complete description.

However, the direction of the maternal blood as it flows upwards from the utero-placental arteries through the cotyledon, through the subchorial blood space, through the circular sinus and back to the uterine vessels, is easily followed. The structure of a cotyledon and the shape of the villous tree is well shown. The outstanding points in Spanner's interpretation of placental anatomy are (1) that the utero-placental arteries, numbering between four and five hundred, communicate with the intervillous space and are evenly distributed over the surface of the placenta while the main venous communications of the intervillous space are at the periphery; (2) that each cotyledon is a unit which may be compared to a box, the boundaries of which do not reach the chorion, so that the maternal blood from all the cotyledons mingles in the subchorial blood lake; (3) the shape of the villous tree may be compared to the shape of an inverted drooping ash. All these facts support the views which Spanner has formulated with regard to the flow of the maternal blood through the placenta.

The material at my disposal includes a 15-day-old ovum obtained at curettage, specimens of non-pregnant uteri obtained at hysterectomy and injected by the gelatin carmine method, one uterus removed at the eighth week of pregnancy and three uteri removed at Cæsarean hysterectomy, one of which was successfully injected by the gelatin carmine method. In addition I have corrosion preparations of the placenta to demonstrate the villous tree.

The technique of injecting material is very difficult and disappointments occur with loss of material. It has taken me fifteen years to collect my material.

The first series of illustrations is devoted to the condition of the endometrium preceding and following implantation of the ovum. It is the arterioles, capillaries and venules of the endometrium which are the important structures with regard to the formation of the placenta and the glands have important mechanical functions but are only concerned with the nourishment of the ovum in an indirect fashion, if at all.

JUNE.—OBSTET. 1

Illustration of Placental Circulation copied from Spanner's Monograph "Mütterlicher und kindlicher Kreislauf der menschlichen Placenta und seine Strombahnen."
(Some details included in his illustration are omitted.)

1. Amnion epithelium. 2-4. Membrana chorii (Chorion plate). 2. Chorion connective tissue. 3. Foetal artery and vein. 4. Chorial trophoblast (or its derivatives). 5. Sub-chorial blood space. 6. Nitabuch's fibrinoid layer. 7. Decidua basalis with many sections of utero-placental whirl artery. 8. Maternal artery. 9. Maternal vein. 10. Muscularis uteri. 11. Peritoneum. 12. White infarct (fibrinoid knot). 13. Cell island (trophoblast). 14. Chorion laeve. A. B. C. Three big anchoring villous trunks to which the Cotyledons *a*, and *b*, limited by septs (4 lower arrows), correspond as well as Marginal Cotyledon *c*. M.Z. Marginal Zone.

Cotyledon *a*.—By leaving out all villi a big villous trunk (A) is shown. The openings of the utero-placental arteries into the intervillous space are seen.

Cotyledon *b*.—Shows Spanner's conception of the branching of the villous tree. The outstanding characteristic of the branching of the villous tree is that the smaller villous trunks run in the form of recurrent loops parallel to each other, running vertically from the basal limits of the placenta towards the chorion. This arrangement of the villous tree brings to mind the picture of an antique chandelier and its candles. Note that the main vessels of the villous trunk (D) run at first into the trophoblast of the basal plate, then turn back and enter (in the form of fine vessels) the central core of villous trunk (D) comes a minor villous trunk which also runs basalwards and is connected by small anchoring villi with the basal plate but finally turns towards the chorion.

Marginal Cotyledon *c*, is concerned with the blood drainage in so much as the intervillous space communicates directly with the uterine veins (arrow), thus the drainage of the venous placental blood is performed by the central sinus (2 upper arrows) in addition to the drainage of blood from the marginal zone directly into the uterine veins.

FIG. 2   FIG. 3   FIG. 4

Fig. 2.—From Bartelmez. A reconstruction of human endometrium in premenstrual stage, showing arterioles, capillaries, venules and glands. [*Amer. J. Obstet. Gynec.*, 1931. 21, 5.] Fig. 3.—Reconstruction from 15-day-old decidua, showing arteriole, dilated capillaries, dilated venules and gland. Fig. 4.—The same to show the position of the implantation cavity and its relationship to the vascular bed.

FIG. 5   FIG. 6

Fig. 5.—Photograph of the injected endometrium of the non-pregnant uterus showing the venules. Muscle, basal, spongy and compact layers are well demonstrated.
Fig. 6.—Photomicrograph showing the arrangement of the capillaries in the compact layer immediately subjacent to the surface of the endometrium. Such is the vascular condition of the endometrium. It is of interest not only for the study of placental circulation but for the study of menstrual and abnormal uterine hæmorrhage.

The next series of illustrations is obtained from an implanted ovum and demonstrates to some extent the early relationships of the implantation cavity to the maternal circulation.
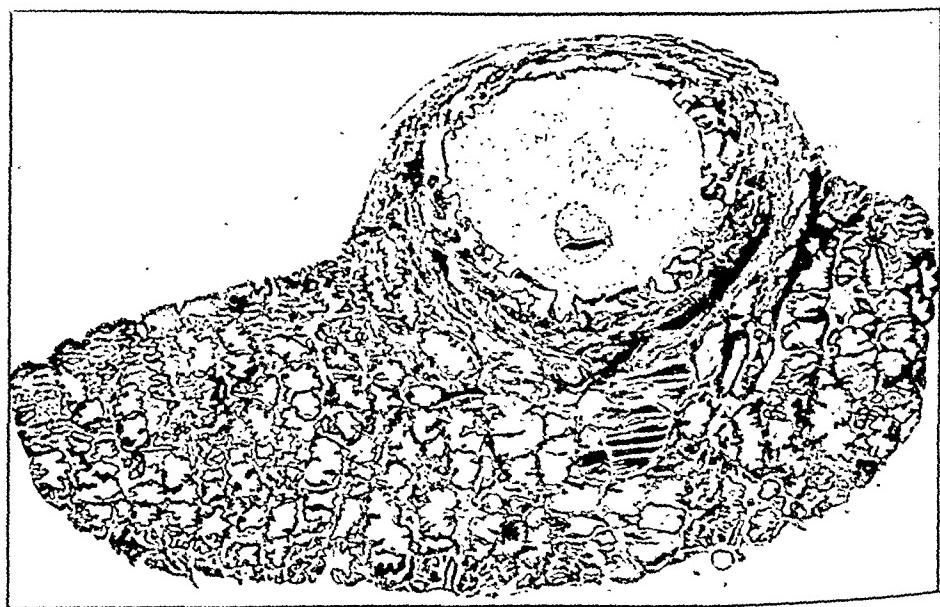
FIG. 7

Fig. 7.—Drawing of a section through the ovum showing the decidua, the chorionic vesicle, the implantation cavity, invaded capillaries, and dilated glands at the base of the ovum.

Implantation cavity   Transition zone   Marginal decidua

FIG. 8

Fig. 8.—Drawing to show a chorionic villus and its attachment to the decidua and the proliferating syncytium passing through the necrotic zone on into the healthy decidua towards and up to a capillary.

FIG. 9
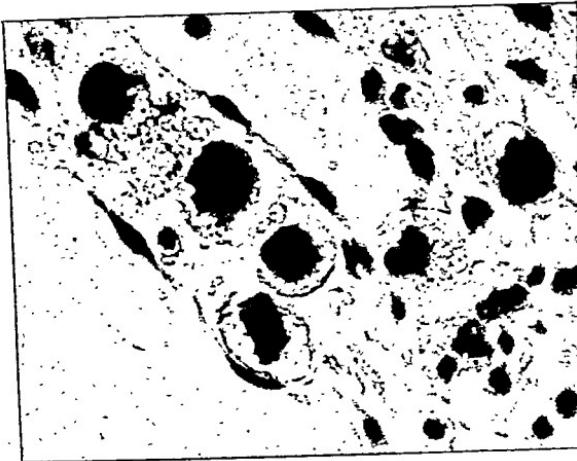
FIG. 11

Fig. 9.—Drawing of the compact decidua showing the secreting endometrium and a capillary with very closely packed endothelial lining cells and a large number of leucocytes in its lumen.

Fig. 10.—Photomicrograph of a corner of the implantation cavity, showing villus; syncytium invaded; syncytium lining venule; venule with cells of the trophoblast replacing the endothelial wall.

Fig. 11.—High power of area marked in fig. 10. This photomicrograph shows the trophoblast actually displacing and replacing one of the endothelial cells lining the maternal vessel and represents the first stage of placentation almost completed.

FIG. 10

Thus as the implantation cavity grows by splitting the decidua it opens up many vascular units consisting of the arteriole and venule described by Bartelmez so that gradually hundreds of arterioles open into the implantation cavity, and eventually become the coiled utero-placental arteries. Spanner holds that the venous return of the placental circulation is almost limited to the periphery of the organ (via the circular sinus). I do not know of any explanation for the disappearance of all the venous channels that must be laid open all over the maternal surface of the placenta.

I have no material which shows the vascular connexions of the placenta in the early months of gestation except one specimen from a hysterectomy. at the 8th week which was injected.

Fig. 12.—Photograph of the pregnant uterus. Shows chorionic villi already limited to one area of the ovum.
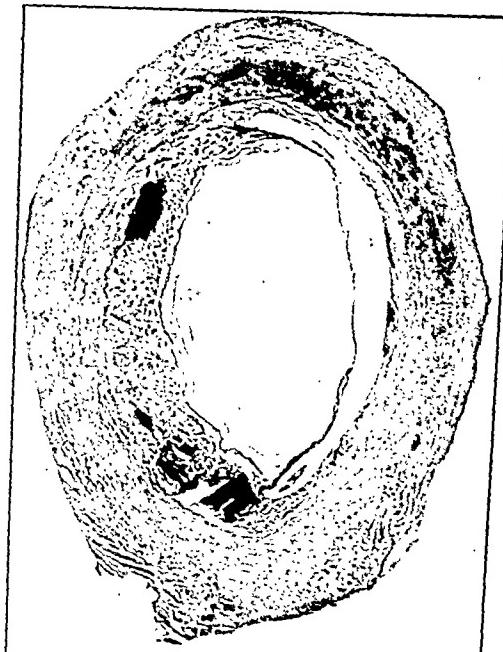
FIG. 12   FIG. 13

The next series of illustrations is concerned with the full-term placenta in situ and is taken from specimens obtained at Cæsarean hysterectomy.

Fig. 13.—Photograph of uterus removed at Cæsarean hysterectomy which was injected through the uterine arteries with gelatin carmine. It has been cut across after fixation to show the placental attachment. Photograph shows the uterine wall, cavity of uterus, placenta attached, site of incision, placenta partially detached.

Fig. 14.—Photograph of section of the same specimen showing uterine wall with placenta attached. Septa, villous trunk, injection material, utero-placental arteries, intervillous space, subchorial blood lake, circular sinus and uterine sinus are all shown.

Fig. 15.—Photomicrograph showing circular sinus and its relationships.

[Figs. 3, 4, 7, 8 and 9 have appeared in *J. Obstet. Gynæc.*, 1932, Vol. 39, No. 3; Figs. 12. 13, 14 and 15 in *Irish J. Med. Sci.*, Feb., 1939, and Figs. 18, 19 and 20 in *Irish J. Med. Sci.*, March, 1942.]
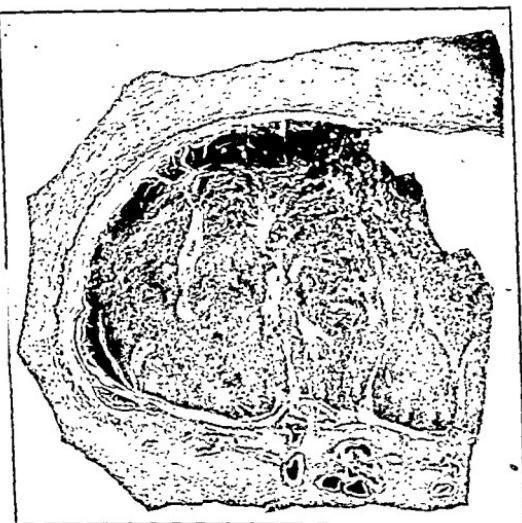
FIG. 14
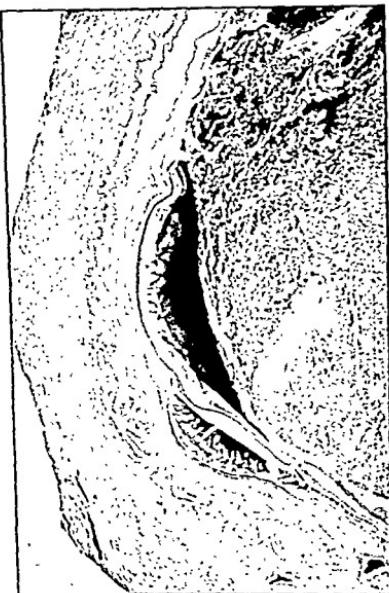
FIG. 15

FIG 16
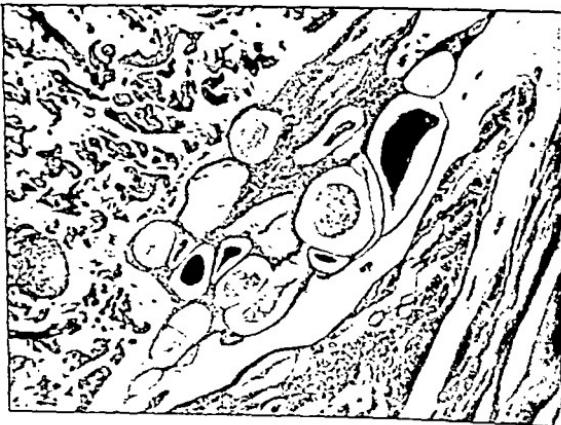
FIG. 17

The next illustrations are taken from a uterus removed in the treatment of placenta prævia—the specimen was not injected.

Fig. 16.—Photograph of a section of the lower segment and cervix showing the low implantation and the opened up circular sinus with maternal blood escaping and passing down the cervix.

Fig. 17.—Photomicrograph of utero-placental coil artery cut across many times.

The remainder of my material is devoted to the fœtal side of the placenta and consists of photographs of corrosion specimens of the full-term placenta and some reconstructions which support Spanner's conception of the villous tree.

FIG. 18

Corrosion preparation. Fœtal surface.

FIG. 19

Maternal surface.

FIG. 20

FIG. 21

Fig. 20.—Corrosion preparation. Fœtal surface, magnified.
Fig. 21.—Reconstruction of villous trunk from gelatin carmine specimen.
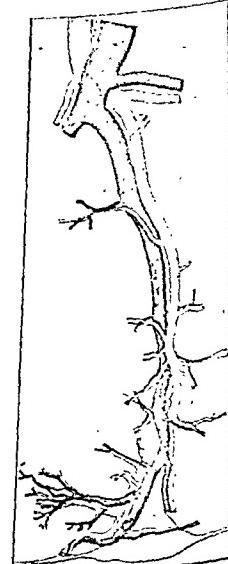
In conclusion I wish to acknowledge the help I have received from Professor Gatenby of the Zoological Department, Trinity College, Dublin, who has allowed me to work in his laboratories. The injection, fixation, sectioning and photography have been done by Mr. D. Glen, the technician in Professor Gatenby's Department. Some of the expenses have been borne by the Irish Medical Research Council, which I gratefully acknowledge.

REFERENCES

BARTELMEZ, G. W. (1931) *Amer. J. Obstet. Gynec.*, **21**, 5.
SPANNER, RUDOLF (1935) *Z. Anat. Entwcklngsgesch.*, **105** (ii), 163.

TWO CASES by J. D. FLEW, M.D., M.R.C.O.G.

The following cases are only related in so far as that they are both the result of mistakes. More might be learnt if our failures, rather than our successes, were more frequently discussed.

(1) Result of Intra-uterine Lipiodol Injection.

The first is the result of an intra-uterine lipiodol performed in the routine investigation of a case of sterility. The radiograph shows a "fluffy" appearance around the body of the uterus, and loops of lipiodol are obvious in the broad ligaments extending upwards in the region of the ovarian vessels.

When I observed this in the wet film, I kept the patient in bed, and twenty-four hours later she developed acute pain in the chest, followed by a small hæmoptysis. During this time she also had severe constant headache, and, three days after the injection, was found to have a left hemiplegia.

Unfortunately no portable X-ray was available, but there seems but little doubt that she had a lipiodol infarction of the lung, and cerebral embolus. Fortunately both these complications cleared up without further extension. She did, however, develop a severe pelvic cellulitis, which kept her in bed for six weeks.

The mistake in this case, performed eight years ago, lay in the fact that the lipiodol injection was carried out some three to four days before the patient's period was expected instead of in the postmenstrual phase, and, as a result, the congested endometrium was eroded by the canula and the lipiodol injected into the blood-stream.

(2) Pre-natal Fracture of Skull.

The second concerns a baby born on May 2, 1942. I was standing by, watching a skilled midwife conduct a twin delivery, the first of which was a breech presentation. All went well until the delivery of the after-coming head, with which there was difficulty, the head being arrested at the pelvic brim. I therefore assisted by suprapubic pressure. The head was delivered without undue trouble by jaw flexion and shoulder traction. The baby was in good condition, but a large depressed fracture of the skull was noticed over the right temporoparietal region.

Some ten hours later I was called because the baby had had a convulsion. By the time I arrived, this had ceased, but the respiratory rate was only 8 per minute, there was cyanosis, and a definite left facial weakness, and left-sided paresis was present. The fontanelle was not unduly tense, and the head was of normal size.

I immediately took the baby to see Mr. Pennybacker at the Radcliffe Infirmary, Oxford, to whom I am indebted for the operation notes.

He agreed with my clinical findings, and under local novocain anæsthesia, operated at once, elevating the depressed fracture.

He then made a small nick in the dura, and found a small subdural hæmorrhage of 3 to 4 c.c. of fluid blood.

The child made an uninterrupted recovery, beating its twin brother, and seventeen days later, the wound was well healed.

The majority of such fractures produce no symptoms, and no neurological signs, and need no treatment. In this case the child might have survived without operation, but Mr. Pennybacker thought there was considerable risk of birth hemiplegia, if not of epilepsy and mental deficiency. The child is now 1 year 8 months old, and is normal in all respects.

[*February* 18, 1944]

Carcinoma Corporis Uteri in Two Sisters Aged 34 and 32 Years.—Anthony W. Purdie, F.R.F.P.S., M.R.C.O.G.

It is comparatively rare to find carcinoma of the body of the uterus in the early thirties.

Sister No. 1, aged 34. Nullipara. Admitted to the North Middlesex County Hospital April 4, 1940, with bleeding of ten days' duration. Pelvic examination showed that the uterus was a little enlarged. To the naked eye the curettings suggested incomplete abortion, but histologically were reported as follows: "An advanced degree of hyperplasia of endometrial glands with necrosis of some fragments. The picture suggests a precarcinomatous condition, but clinical review of the case from time to time will probably eliminate this."

Normal menstruation continued, except that in August she bled for one month. In November and December bleeding became irregular, and further curettage in January 1941 showed endometrial carcinoma. Total hysterectomy with left salpingo-oöphorectomy was performed (previously she had had a right-sided ovarian cyst removed) followed by deep X-rays. She has been well ever since. The uterus when sectioned showed "an endometrial carcinoma of well-differentiated structure, slowly invading the uterine wall. The ovary and tube show no involvement by the growth".

Sister No. 2, age 32. Nullipara. Admitted October 16, 1942, with vaginal bleeding for one week. Her periods had never been regular. Pelvic findings were normal. Diagnostic curettage yielded a piece of tissue suggestive either of incomplete abortion or corporeal carcinoma. Histology proved it to be the latter. Total hysterectomy with bilateral salpingo-oöphorectomy was performed, followed by deep X-rays. She has been well ever since. Histological examination of the uterus confirmed the carcinomatous nature of the endometrium and showed moderate penetration of the uterine musculature.

Family history.—The patients' mother had ten children. One sister died of meningitis at 10 months. The rest are alive and well. Recently Mr. Alan Brews (1943, personal communication) performed a hysterectomy on one of their sisters for a benign condition.

Their mother died of cancer of the rectum at 68, and two maternal uncles died of cancer of other organs.

Discussion

Corporeal carcinoma is typically a post-menopausal condition. The largest number of cases occurs in the sixth decade. It is surprising how many observers find the average age within the narrow limits of 56 to 58 years.

Of great interest is its occurrence in children (*see* Hirst, 1929; Morse, 1930, quoting Kehrer and Neumann, 1928; and Gilbert, 1932).

The other aspect is familial occurrence (*see* Williams, 1898; Auvray, 1927; and Imamura, 1938).

While possible familial tendency to carcinoma in the same organ is of speculative interest, these two cases emphasize a point of great practical importance—the possible occurrence of carcinoma corporis uteri in comparatively young women.

My thanks are due to Dr. H. Rogers, Pathologist to the North Middlesex County Hospital.

REFERENCES

AUVRAY (1927) *J. Amer. med. Ass.*, 88, 1579.
GILBERT, J. B. (1932) *Amer. J. Obstet. Gynec.* 24, 402.
HIRST, B. C. (1929) *Amer. J. Obstet. Gynec.*, 18, 104.
IMAMURA, S. (1938) *Jap. J. Obstet. Gynec.*, 21, 127.
MORSE, A. H. (1930) *Amer. J. Obstet. Gynec.*, 19, 520.
WILLIAMS, W. R. (1898) *Brit. med. J.* (ii), 1612.

Gaertner's Cyst.—C. Scott Russell, F.R.C.S.Ed.

About thirteen years ago a mother noticed that her baby daughter, then aged 3, was slightly wet during the day. This puzzled her if only because the child never had a wet bed at night. Her doctor assured her that all would be well in time, the child was thriving, so nothing further was done.

At the age of 16, she was referred to hospital as the slight escape of water had persisted. She was dry in bed at night, but during the day the loss was enough to damp her knickers or one sanitary pad; the symptom did not distress her unduly. Inspection of the vulva showed no abnormality. On examination under anæsthesia a small cyst was found in the lower third of the anterior vaginal wall. Pressure on this cyst resulted in the escape of a tiny quantity of fluid from a minute aperture alongside the external meatus. A probe passed into this opening demonstrated a short tract, but no connexion between it and the urethra or the vaginal cyst could be made out. The bladder, which the girl

had always been able to empty voluntarily, looked normal and there was no abnormal pelvic swelling.

Diodone was injected into the opening alongside the urethral meatus, and subsequent X-ray films outlined the vaginal cyst showing that it was in fact continuous with the external opening. In addition the films showed that the vaginal cyst was continuous with a much larger cyst that extended far backwards in the pelvis. X-ray films following uroselectan intravenously showed normal kidney and ureteric shadows on each side.

Some weeks later a further examination was made in order to localize this cavity as accurately as possible. Ureteric catheters were passed, the cyst was again injected with diodone, and iodized oil was injected into the uterus and fallopian tubes. Stereoscopic X-ray films made it possible to trace the upward extension of this cyst. The palpable part lay between bladder and vagina—the pelvic extension passed backwards and laterally between ureter and lower part of the uterus, then internal to the R. ischial spine and behind the ureter which was pushed forwards and medially, then close to the upper part of the sacrum, where it turned abruptly downwards to finish at a slightly lower level.

This girl is hardly inconvenienced by the escape of fluid; any surgical operation to remove the cyst and its ramifications would be a formidable procedure.

Two Granulosa-celled Tumours.—E. FRIEDMANN, M.D.

The first case was a girl of 11, first seen in 1936. The first vaginal hæmorrhage occurred at 9 years of age, and by 11 she had developed full secondary sex-characters. She was admitted for severe floodings and extreme anæmia.

Examination showed bilobular swelling up to the umbilicus which on operation was found to be a uterus the size of at least 16 weeks' pregnancy and an irregular, semi-solid, greyish tumour, the size of a fœtal head. Microscopically it was a granulosa-celled tumour of follicular type with only a few cylindromatous areas.

I saw the girl eight years later at the age of 19. She had not developed further except for weight and features. Her periods were regular, very scanty, and the uterus much smaller than normal. The enormous over-production of œstrone which at the age of 11 had caused the extreme hypertrophy of uterus—the largest ever recorded—had apparently depressed the pituitary so much that full recovery had not taken place.

The second was a thin, frail, anæmic woman of 74, nullipara; menopause twenty-seven years ago; bled for several months and lost weight. She had a fairly firm tumour, apparently continuous with the cervix, believed to be an anteverted bulky uterus. B.P. 160/100.

A diagnostic dilatation and curettage without anæsthetic, owing to her debility, produced no scrapings, but the bleeding stopped. Four weeks later she was admitted to the Royal Free Hospital for rather serious hæmorrhages. Laparotomy showed a diverted, partly cystic, partly stony-hard, nodular ovarian tumour and a very tiny uterus hidden and flattened by the tumour, which was a granulosa-celled tumour of the follicular and cylindromatous type. It was a senile uterus with no hypertrophy of the muscle or the slightest hyperplasia of endometrium. Only cervical glands were found.

Apparently it is possible for a granulosa-celled tumour to be active without affecting endometrium and uterine muscle although hyperplasia is supposed to be a constant finding both in benign and malignant cases.

A Case of Ovarian Dysgerminoma.—DONALD FRASER, F.R.C.S.

A married woman of 36, with two children, had secondary amenorrhœa. Five and a half years previously her periods suddenly ceased. Eleven months later her second child was born, which she breast-fed for one year. After this she had four periods lasting one day, at two-monthly intervals, and finally the periods ceased altogether for a year and a half.

On general examination there was no virilism or other abnormality. Locally a tumour was felt in the region of the left ovarian appendage. Aschheim-Zondek test was negative and ketosterol excretion normal.

The soft encapsulated tumour, removed at operation, was 3 in. in diameter and cut like brain tissue. Section was reported by Professor Hadfield as ovarian dysgerminoma. Four weeks after its removal the periods returned and for the past year have remained regular with a new cycle of twenty-four days and loss of seven days.

It appears obvious that the tumour was producing an inhibitory hormone which in some way stopped menstruation.

Uniovular Triplets.—LILIAN RAFTERY, M.R.C.O.G., M.M.S.A.

Multiparous woman, aged 32. The first child born seven years previously; normal confinement. Her husband's mother and sister had both had twins. There was no maternal history of multiple pregnancy.

This pregnancy, dating from last menstrual period on 30.10.42, was normal until the 30th week of gestation when she complained of the abnormally large size of her abdomen. Clinical examination at that time suggested a twin pregnancy and X-ray revealed the presence of triplets. The blood-pressure was 100/75, there was a haze of albumin in a catheter specimen and pitting œdema to the knees. The abdominal girth was 42 in. She was admitted to hospital and received a full pregnancy diet, with additional iron, calcium and vitamins. The blood-pressure remained low and the œdema and albuminuria subsided.

Labour began, 16.7.43, with the rupture of the membranes, and three female children were born. The first spontaneous birth was as a full breech, the second, also spontaneous, as a face to pubis and the third as an incomplete breech with extended legs, without assistance. The whole labour lasted only eleven hours, and there was no post-partum hæmorrhage or collapse. The children weighed 4 lb. 5 oz., 4 lb. 6 oz., and 4 lb. 15 oz., respectively. The placenta was uniovular, all areas connected by blood-vessels and with no evidence of infarction.

One hour after delivery, the patient complained of a headache and was found to have generalized œdema and a blood-pressure of 185/100, with only a trace of albuminuria. Three hours after delivery, she had an eclamptic fit. However, she responded well to treatment, and two days later, all œdema and albuminuria had disappeared and the blood-pressure was 140/90. Breast feeding of all three children was successfully carried out.

The infants are of identical appearance; the latest photograph looks like three poly-photographs of the same child. Their blood groups were all Group O, like the mother, and the other stigmata, colour of iris, colour of hair, shape of eyes and ears were so similar that the mother herself has difficulty in distinguishing between Jean, Janet and Jennifer.

Following up the investigations of Bak in Budapest, I had the babies' fingerprints examined, through the courtesy of Scotland Yard. Unlike the results from Budapest, where very similar, though no identical, fingerprints were obtained in the cases of uniovular twins, our investigations showed that the three sets of fingerprints were totally dissimilar. In fact, the three children demonstrated three of the four broad groups of fingerprints commonly found.

The points of interest in this case are: (1) The paternal history of multiple pregnancies; (2) the quick spontaneous labour; (3) the post-partum increase of the slight antenatal toxæmia to eclampsia; (4) the successful lactation and breast feeding; (5) the extreme dissimilarity of the fingerprints in triplets proved uniovular by physical characteristics and careful placental examination.

Retroverted Gravid Uterus Associated with Gross Retention of Urine.—Doreen Daley, M.D., M.R.C.O.G.

History.—A woman, aged 39, who had had six normal pregnancies, was admitted to hospital on 29.5.43 on account of abdominal swelling. For the previous three weeks she had had to strain to pass urine. Micturition had been painful and frequent. She had not been incontinent. The abdominal distension was noticed about a week after the onset of symptoms and a week later her legs and vulva had started to swell. She had not vomited and said that her bowels had been opened each day. Following a normal menstrual cycle she had had fourteen weeks' amenorrhœa.

On examination.—T. 97·4; P. 68; R. 20. Breathing laboured. Obviously in pain. Heart and lungs normal. B.P. 160/98. Blood urea 44 mgm.%. Abdomen filled by a tense, tender, cystic tumour. No evidence of fœtal parts. Legs and thighs markedly œdematous. Vaginal examination: Labia very swollen. Rectum loaded with hard fæces. Cervix difficult to reach but appeared to be high under the symphysis with the uterus retroverted.

Progress.—By means of a self-retaining catheter with a screw-clip, urine was drained until the bladder was emptied. Thirty-three pints were collected in fifty-three hours. During this time the fluid intake was nine pints. The urine contained a trace of albumin, pus and enterococci but no red cells or casts. Sp. gr. 1004-1008. After the catheter was removed, she did not have any further difficulty with micturition. The uterus could be palpated *per abdomen* as soon as the bladder was empty and corresponded in size with a 14 weeks' pregnancy. Œdema rapidly disappeared and blood pressure and blood urea fell to normal. She was discharged thirteen days after admission and thereafter had a normal pregnancy, labour at term and puerperium. The uterus was retroverted when she was examined six weeks after delivery.

Spontaneous Reduction of the Inverted Uterus.—C. K. Vartan, F.R.C.S.

Spontaneous reduction was recorded by Meigs in 1863 and by Spiegelberg of Berlin in 1887. In 1904 Dr. Robert Boxall recorded a case which occurred after

to replace it had failed. In discussing this case, Dr. Herbert Spencer quoted a case occurring five weeks after delivery. He stated that Sir John Williams knew of a similar case. In 1912 Hoover advocated leaving the inversion alone and treating only the shock.

To Sir Comyns Berkeley goes the distinction of being the first to leave the uterus alone, deliberately—confident that it would go back unaided. He had seen this occur in a previous case while waiting for an Aveling's repositor. He recorded this case at this Society in 1915. In 1925 McCullagh added another. In 1929, Mr. Miles Phillips, who has very kindly sent me a personal communication on this subject, records a case. The uterus was septic on admission, was treated with glycerine and glauramine and blood was transfused. He saw the uterus reducing itself on the nineteenth day, and observed its completion on the twentieth. Barrows in 1934 records an inverted uterus discovered eight weeks after delivery in which attempted replacement was unsuccessful. Tampons and douches were given for two weeks as a pre-operative measure, and it was then found that spontaneous reduction had taken place. Onslow records a similar instance in 1936, and in 1938 Brett gives two instances occurring seven weeks after delivery. To these cases I add one more. For the details of the delivery I am indebted to Dr. J. D. Evans of Eltham whose patient she was.

Mrs. F., a primipara, was delivered with forceps under chloroform anæsthesia of a child weighing 7¼ lb. There was no interference in the third stage and neither pituitrin nor ergot was given, but the uterus with the placenta attached spontaneously inverted on to the bed. Hæmorrhage was "considerable but not alarming". The placenta separated spontaneously and the patient only then collapsed. Stimulants were given, and an infusion of 500 c.c. of 5% glucose saline was started. An attempt at reduction was made but the patient collapsed again, and having got the uterus back into the vagina nothing further was done. I saw the patient ten hours later and though she was pale she was no longer shocked. B.P. was 110/80.

In the abdomen the tightly constricted cervical ring was easily felt, 2 in. above the symphysis, and the vagina contained the whole of the inverted uterus. It seemed almost folly to attempt to get so large a mass through so small a ring and no more than a tentative attempt was made. A full course of sulphathiazole (20 g.) was started, and the patient was removed to hospital. The hæmoglobin on admission was 36%, and the R.B.C. 1·9 millions. Two pints of blood were transfused.

She was then ordered "Fersolate" tabs. 2, t.d.s., together with vitamins A, B, C, and D in appropriate dosage. Three days later the hæmoglobin was 56%, and breast feeding was started.

Five days after delivery, a spinal anæsthetic was given and an attempt at replacement was made. No success attended this and the risk of doing more harm than good was clear. The uterus was therefore painted with Bonney's blue, and the patient was returned to the ward. An Aveling's repositor was ordered, but at some stage during the ensuing twenty days the uterus returned to its normal situation, for, when the repositor arrived and was to be fitted, the pelvis was quite normal.

For the first three days the temperature was 100°, but subsequently it rarely rose above 99°. The last hæmoglobin reading was 65%. Thus she returned home on the twenty-ninth day with a normal pelvis, and a baby thriving, and well established at the breast.

Many writers show that immediate replacement can be successfully effected, but most add that in the presence of shock this should not be attempted. This is borne out by the high mortality which attends the practice. That there are so few recorded cases of spontaneous reduction is undoubtedly due to the fact that in most cases interference takes place. The following measures are recorded:

Accidental avulsion; immediate amputation and delayed amputation; replacement by central, and by peripheral taxis; abdominal salpingo-oöphorectomy combined with vaginal hysterectomy; abdominal manipulation, with and without simultaneous manipulation *per vaginam*; Spinelli's posterior colpo-hysterotomy; incision of the posterior ring *per abdomen*; extraction of the inverted uterus *per abdomen* with Allis's forceps. All these operations are formidable and by no means all of the patients have survived. Replacement with Aveling's repositor is sometimes successful. McLennan and McKelvie (1942) pointing out that some of the inverted uteri will go back spontaneously, express the opinion that the textbook treatment is not necessarily the treatment of choice, and they strongly urge doing nothing which might increase the shock, advocating instead transfusion and sulphanilamide therapy; and sober review of the situation in from four to six weeks' time.

Mr. Miles Phillips goes so far as to say that a case stands a better chance of recovery undiagnosed than one operated on while shock is still present.

To these views I subscribe, and add my belief that in the case I have presented, breast feeding of the infant aided the involution and appreciably shortened the convalescence.

This pregnancy, dating from last menstrual period on 30.10.42, was normal until the 30th week of gestation when she complained of the abnormally large size of her abdomen. Clinical examination at that time suggested a twin pregnancy and X-ray revealed the presence of triplets. The blood-pressure was 100/75, there was a haze of albumin in a catheter specimen and pitting œdema to the knees. The abdominal girth was 42 in. She was admitted to hospital and received a full pregnancy diet, with additional iron, calcium and vitamins. The blood-pressure remained low and the œdema and albuminuria subsided.

Labour began, 16.7.43, with the rupture of the membranes, and three female children were born. The first spontaneous birth was as a full breech, the second, also spontaneous, as a face to pubis and the third as an incomplete breech with extended legs, without assistance. The whole labour lasted only eleven hours, and there was no post-partum hæmorrhage or collapse. The children weighed 4 lb. 5 oz., 4 lb. 6 oz., and 4 lb. 15 oz., respectively. The placenta was uniovular, all areas connected by blood-vessels and with no evidence of infarction.

One hour after delivery, the patient complained of a headache and was found to have generalized œdema and a blood-pressure of 185/100, with only a trace of albuminuria. Three hours after delivery, she had an eclamptic fit. However, she responded well to treatment, and two days later, all œdema and albuminuria had disappeared and the blood-pressure was 140/90. Breast feeding of all three children was successfully carried out.

The infants are of identical appearance; the latest photograph looks like three poly-photographs of the same child. Their blood groups were all Group O, like the mother, and the other stigmata, colour of iris, colour of hair, shape of eyes and ears were so similar that the mother herself has difficulty in distinguishing between Jean, Janet and Jennifer.

Following up the investigations of Bak in Budapest, I had the babies' fingerprints examined, through the courtesy of Scotland Yard. Unlike the results from Budapest, where very similar, though no identical, fingerprints were obtained in the cases of uniovular twins, our investigations showed that the three sets of fingerprints were totally dissimilar. In fact, the three children demonstrated three of the four broad groups of fingerprints commonly found.

The points of interest in this case are: (1) The paternal history of multiple pregnancies; (2) the quick spontaneous labour; (3) the post-partum increase of the slight antenatal toxæmia to eclampsia; (4) the successful lactation and breast feeding; (5) the extreme dissimilarity of the fingerprints in triplets proved uniovular by physical characteristics and careful placental examination.

Retroverted Gravid Uterus Associated with Gross Retention of Urine.—Doreen Daley, M.D., M.R.C.O.G.

History.—A woman, aged 39, who had had six normal pregnancies, was admitted to hospital on 29.5.43 on account of abdominal swelling. For the previous three weeks she had had to strain to pass urine. Micturition had been painful and frequent. She had not been incontinent. The abdominal distension was noticed about a week after the onset of symptoms and a week later her legs and vulva had started to swell. She had not vomited and said that her bowels had been opened each day. Following a normal menstrual cycle she had had fourteen weeks' amenorrhœa.

On examination.—T. 97·4; P. 68; R. 20. Breathing laboured. Obviously in pain. Heart and lungs normal. B.P. 160/98. Blood urea 44 mgm.%. Abdomen filled by a tense, tender, cystic tumour. No evidence of fœtal parts. Legs and thighs markedly œdematous. Vaginal examination: Labia very swollen. Rectum loaded with hard fæces. Cervix difficult to reach but appeared to be high under the symphysis with the uterus retroverted.

Progress.—By means of a self-retaining catheter with a screw-clip, urine was drained until the bladder was emptied. Thirty-three pints were collected in fifty-three hours. During this time the fluid intake was nine pints. The urine contained a trace of albumin, pus and enterococci but no red cells or casts. Sp. gr. 1004–1008.

After the catheter was removed, she did not have any further difficulty with micturition. The uterus could be palpated *per abdomen* as soon as the bladder was empty and corresponded in size with a 14 weeks' pregnancy. Œdema rapidly disappeared and blood-pressure and blood urea fell to normal. She was discharged thirteen days after admission and thereafter had a normal pregnancy, labour at term and puerperium. The uterus was retroverted when she was examined six weeks after delivery.

Spontaneous Reduction of the Inverted Uterus.—C. K. Vartan, F.R.C.S.

Spontaneous reduction was recorded by Meigs in 1863 and by Spiegelberg of Berlin in 1887. In 1904 Dr. Robert Boxall recorded a case which occurred after two attempts

to replace it had failed. In discussing this case, Dr. Herbert Spencer quoted a case occurring five weeks after delivery. He stated that Sir John Williams knew of a similar case. In 1912 Hoover advocated leaving the inversion alone and treating only the shock.

To Sir Comyns Berkeley goes the distinction of being the first to leave the uterus alone, deliberately—confident that it would go back unaided. He had seen this occur in a previous case while waiting for an Aveling's repositor. He recorded this case at this Society in 1915. In 1925 McCullagh added another. In 1929, Mr. Miles Phillips, who has very kindly sent me a personal communication on this subject, records a case. The uterus was septic on admission, was treated with glycerine and glauramine and blood was transfused. He saw the uterus reducing itself on the nineteenth day, and observed its completion on the twentieth. Barrows in 1934 records an inverted uterus discovered eight weeks after delivery in which attempted replacement was unsuccessful. Tampons and douches were given for two weeks as a pre-operative measure, and it was then found that spontaneous reduction had taken place. Onslow records a similar instance in 1936, and in 1938 Brett gives two instances occurring seven weeks after delivery. To these cases I add one more. For the details of the delivery I am indebted to Dr. J. D. Evans of Eltham whose patient she was.

Mrs. F., a primipara, was delivered with forceps under chloroform anæsthesia of a child weighing 7¼ lb. There was no interference in the third stage and neither pituitrin nor ergot was given, but the uterus with the placenta attached spontaneously inverted on to the bed. Hæmorrhage was "considerable but not alarming". The placenta separated spontaneously and the patient only then collapsed. Stimulants were given, and an infusion of 500 c.c. of 5% glucose saline was started. An attempt at reduction was made but the patient collapsed again, and having got the uterus back into the vagina nothing further was done. I saw the patient ten hours later and though she was pale she was no longer shocked. B.P. was 110/80.

In the abdomen the tightly constricted cervical ring was easily felt, 2 in. above the symphysis, and the vagina contained the whole of the inverted uterus. It seemed almost folly to attempt to get so large a mass through so small a ring and no more than a tentative attempt was made. A full course of sulphathiazole (20 g.) was started, and the patient was removed to hospital. The hæmoglobin on admission was 36%, and the R.B.C. 1·9 millions. Two pints of blood were transfused.

She was then ordered "Fersolate" tabs. 2, t.d.s., together with vitamins A, B, C, and D in appropriate dosage. Three days later the hæmoglobin was 56%, and breast feeding was started.

Five days after delivery, a spinal anæsthetic was given and an attempt at replacement was made. No success attended this and the risk of doing more harm than good was clear. The uterus was therefore painted with Bonney's blue, and the patient was returned to the ward. An Aveling's repositor was ordered, but at some stage during the ensuing twenty days the uterus returned to its normal situation, for, when the repositor arrived and was to be fitted, the pelvis was quite normal.

For the first three days the temperature was 100°, but subsequently it rarely rose above 99°. The last hæmoglobin reading was 65%. Thus she returned home on the twenty-ninth day with a normal pelvis, and a baby thriving, and well established at the breast.

Many writers show that immediate replacement can be successfully effected, but most add that in the presence of shock this should not be attempted. This is borne out by the high mortality which attends the practice. That there are so few recorded cases of spontaneous reduction is undoubtedly due to the fact that in most cases interference takes place. The following measures are recorded:

Accidental avulsion; immediate amputation and delayed amputation; replacement by central, and by peripheral taxis; abdominal salpingo-oöphorectomy combined with vaginal hysterectomy; abdominal manipulation, with and without simultaneous manipulation *per vaginam;* Spinelli's posterior colpo-hysterotomy; incision of the posterior ring *per abdomen;* extraction of the inverted uterus *per abdomen* with Allis's forceps. All these operations are formidable and by no means all of the patients have survived. Replacement with Aveling's repositor is sometimes successful. McLennan and McKelvie (1942) pointing out that some of the inverted uteri will go back spontaneously, express the opinion that the textbook treatment is not necessarily the treatment of choice, and they strongly urge doing nothing which might increase the shock, advocating instead transfusion and sulphanilamide therapy; and sober review of the situation in from four to six weeks' time.

Mr. Miles Phillips goes so far as to say that a case stands a better chance of recovery undiagnosed than one operated on while shock is still present.

To these views I subscribe, and add my belief that in the case I have presented, breast feeding of the infant aided the involution and appreciably shortened the convalescence.

REFERENCES

BARROWS (1934) *Amer. J. Obstet. Gynec.*, 27, 105.
BERKELEY, COMYNS (1915) *Proc. R. Soc. Med.*, 8, Sect. Obstet., 56.
BOXALL, R. (1904) *Trans. obstet. Soc. Lond.*, 46, 292.
BRETT (1938) *Med. J. Aust.* (i), 254.
McCULLAGH, W. McH. (1925) *J. Obstet. Gynec.*, 32, 280.
McLENNAN and McKELVIE (1942) *J. Amer. med. Ass.*, 120, 679.
MEIGS, C. D. (1863) Obstetrics, the Science and Art, Philadelphia.   4th Ed.
ONSLOW, GORDON Jr. (1936) *Amer. J. Obstet. Gynec.*, 32, 398.
PHILLIPS, MILES (1929) *Clin. J.*, 58, 205.
SPIEGELBERG (1887) Textbook of Midwifery, London.

A Case of Spontaneous Annular Detachment of the Cervix During Labour.—M. DAVIES WESTERMAN, M.B., B.S.

The patient was a healthy primigravida aged 27. She was short and fat and had a flat type of pelvis. As she approached term the fœtal head remained high and she was booked for a trial labour in Shardeloes Maternity Hospital, Amersham.

Two weeks after the expected date of delivery the patient went into labour following spontaneous rupture of membranes. Presentation V.R.O.P. head high. The first stage progressed normally apart from difficulties arising out of her very unco-operative behaviour and in twelve hours the head was engaged; after twenty-four hours her pulse-rate began to rise although her general condition was good. Despite morphia and a good night's rest her pulse rose gradually to 110. This rate was maintained till after delivery. The rhythm was always regular and the volume good except for a period of five minutes, five hours before the second stage began, when it became irregular and thready.

There were no other abnormal signs during the first stage which lasted forty-three hours.

The second stage: After one hour of poor pains and no advance it was decided to terminate with forceps.

The head was found well down and arrested in the transverse and was easily rotated. During this manœuvre a loose band of œdematous tissue was felt between the head and the sacrum. On further investigation this proved to be the prolapsed anterior cervical lip; the cervix having sloughed round the anterior two-thirds of its circumference, the head was presenting through the rent. There were multiple loops of cord round the child's neck which were pulsating slowly. As the vital part of the cervix had already separated, only the posterior third being left attached, it was considered that the danger of hæmorrhage from the uterine arteries, and tearing into the vaginal vaults was now over. Forceps were therefore applied to the head, through the rent, above the ring of the detached cervix. An 8 lb. stillborn baby was easily delivered, the detached cervix being borne in front of the head, the posterior third separating when traction was applied.

The third stage and puerperium were uneventful. The patient discharged herself on the fourteenth day. On examination before discharge a smooth regular cervical stump was palpated. Speculum examination was impossible to perform as the patient would not co-operate. No cause was found for the stillbirth.

Meigs' Syndrome.—MARY KATHLEEN LAWLOR, M.R.C.S., M.R.C.O.G.

A number of cases of ovarian fibroma associated with ascites and hydrothorax have been reported in recent years by J. V. Meigs, and the following case is similar to those in Meigs' series.

A patient, aged 35, married, nulliparous, was admitted to hospital, complaining of breathlessness and abdominal enlargement of twelve months' duration, but with an increase in the severity of the symptoms for the previous two weeks.

On examination, there were signs of a massive effusion of the right side of the chest, with a mediastinal shift to the left. The apex beat was 5 in. from the mid-line in the 5th intercostal space, but there was no other cardiac abnormality. The X-ray picture confirmed these findings. The abdominal girth measured 38 in. and there was a firm mass palpable in the left iliac fossa extending upwards to the level of a 20 weeks' cyesis.

Ten pints of fluid were withdrawn from the right pleural cavity, in order to improve the condition before operation. Air entry was then detected to the level of the angle of the scapula and confirmed by X-ray. A laparotomy revealed a simple ovarian fibroma with a moderate degree of ascites. Torsion of the pedicle had taken place. The left ovary and tumour were removed. No other abnormality in the abdomen was seen and the diaphragm showed no signs of an aperture.

Following the operation the patient made an uninterrupted recovery with spontaneous absorption of the pleural effusion. Six days later no fluid could be detected in the chest, and eight days after operation the X-ray showed no effusion visible. Discharge from hospital took place on the eighteenth day and when seen four months later and again four years later, there was no return of the symptoms.

[*March* 17, 1944]

DISCUSSION ON CHRONIC VULVAL SKIN LESIONS

Mr. Victor Bonney recalled that in 1904 he began a research into the connective tissues in carcinoma and antecedent states. An interim report was made in 1907 in the Report of the Middlesex Hospital Cancer Investigation Laboratories, and in 1908 the results of the full research formed the subject of the three Hunterian Lectures he gave at the Royal College of Surgeons.

The gist of his results was that in all sites of carcinoma malignant down-growth of epithelium was preceded by profound changes in the connective tissue underlying the epithelium, or in other words that malignant down-growth of epithelium never primarily took place into healthy connective tissue.

In studying carcinoma of the vulva he soon became aware that *in almost all cases the malignant disease was superadded to pre-existent leukoplakia.* This connexion had been pointed out by Hulke many years before but no research had been based on it. He (V. B.) coined the appellation "Leukoplakic Vulvitis" to describe what was from the start an inflammatory change, and he distinguished three stages: an early stage where the subepithelial tissue became flooded by inflammatory cells, chiefly lymphocytes and the epithelium was proliferating rapidly; a middle stage where the subepithelial tissue had largely lost its collagen fibres and its yellow elastic fibres entirely, while the epithelium, greatly hypertrophied, formed deeply penetrating interpapillary processes and exhibited intense surface keratinization, whence the white appearance. In this stage fissures, erosions and warty elevations appeared and it was in such that the earliest histological evidence of malignant epithelial invasion was to be found.

If this danger was escaped a third stage was entered on where the subepithelial tissue became densely fibrous again and the epithelium, still heavily keratinized, tended to become a flat sheet. By this time the pruritus characteristic of the disease had often stopped altogether and the patient ceased to complain but there was no return of the tissues to their normal state.

In 1909 he and Sir Comyns Berkeley read a paper before the Section on Leukoplakic Vulvitis and its Relation to Carcinoma Vulvæ, Berkeley doing the clinical aspects while his research supplied the pathological details (*Proc. R. Soc. Med.*, 3, Sect. Obstet., 29).

In this paper Berkeley and he drew a distinction between leukoplakic vulvitis and that atrophic condition marked by shrinkage and very tender red patches around the vaginal introitus, urinary meatus and vestibule. Previously they had been considered as different manifestations of the same disease and were called white and red kraurosis. They pointed out that in symptoms, distribution and histopathological structure they were entirely different, and suggested that the term kraurosis should be limited to what had been called red kraurosis, whilst white kraurosis should in future be known as leukoplakic vulvitis.

There were many conditions causing vulval pruritis and amongst them some which were liable to be mistaken for leukoplakic vulvitis on account of their whitish appearance. He himself had described one of these ("Lepidosis Vulvæ", *Proc. Roy. Soc. Med.*, 31, 1058), but the dermatologists apparently held that leukoplakic vulvitis was their old friend lichen planus masquerading under another name, though there was no likeness between the two. Lichen planus was a patchy disease having no specific distribution. Leukoplakic vulvitis was not patchy but affected a whole area from the start and this area had a characteristic distribution, namely the hood of the clitoris, the labia minora and the fourchette. Occasionally it was true that the itchy area extended back around the anus but even then the changes in the perineal and perianal skin were histologically different from those of the vulva, and more resembled those found in primary pruritus ani. Of the very large number of cases of leukoplakic vulvitis that he had seen any coincident affection of the skin of the body at large was exceedingly rare but with lichen planus the very reverse was the case. The lesions of lichen planus could be entirely recovered from, not only symptomatically but histologically, while in leukoplakic vulvitis histological cure never took place, the tissues affected being permanently altered.

Finally, leukoplakic vulvitis tended to become carcinomatous while there was no such tendency with lichen planus. Leukoplakic vulvitis and kraurosis vulvæ formed two clear-cut entities with which every gynæcologist was familiar. He appealed to dermatologists to accept the labels given by gynæcologists to describe these two separate conditions and so clear up what up to the present time was a depressing muddle.

Dr. R. T. Brain : It is by no means certain that a group of cases having similar clinical features have a common pathological basis, even though the histological features may be very similar, as, indeed, one would expect them to be. The reaction of the skin, as in the case of other organs, is chiefly manifest by the well-known features of inflammation, and so it is that many chronic inflammatory lesions of the skin present similar-

ities which do not allow the most expert pathologist to make a diagnosis with any more confidence than his clinical confrère.

The first lesion to consider is lichen simplex, which is usually regarded as a neurogenic lesion resulting from prolonged scratching. Thus, every case of pruritus vulvæ is bound to be complicated by some of the features of lichenification which is made manifest by a general thickening of the skin, presumably because repeated trauma maintains a chronic inflammatory condition, and the friction and the dilatation of vessels account for hypertrophy of the epidermis. Histologically this is shown by acanthosis, enlarged papillæ produced by down-growths of the epidermis, and various degrees of œdema and infiltration of the papillæ and the underlying dermis. Hyperkeratosis may be marked. Clinically, lichen simplex is recognized as a well-defined area of dull red or brownish red colour with marked exaggeration of the normal grooves of the skin, which divide the thickened area into lozenge-shaped, flat papules. When the skin surface is moist, the increased horny scale is macerated and whitened and the appearances are indistinguishable from those described by Bonney in 1938, which he termed lepidosis vulvæ.

Chronic irritation of the skin by external factors such as irritating discharges and recurrent mild infections may produce very similar appearances, and they are the secondary features of many cases of chronic dermatitis and eczema, very familiar to dermatologists.

Psoriasis of the vulva may closely simulate lichen simplex and since pruritus is common at this site some degree of lichenification is usually superimposed upon the psoriasis. However, the eruption precedes the symptoms, the colour is a brighter red and the skin surface shiny, with a thin, closely adherent scale which shows silvery lines when lightly scratched. The mons veneris is often first affected and the lesion then extends over the external surfaces of the labia majora to the perineum and anal region, and may involve the whole gluteal cleft. Psoriasis rarely affects the mucous surfaces but instances have been reported; mostly buccal lesions similar to those about to be described in lichen planus. The diagnosis may be facilitated if characteristic lesions are found on other parts of the body and thimble-like pittings of the nails and subungual hyperkeratosis may give helpful clues.

Seborrhœic dermatitis somewhat resembles the flexural type of psoriasis and may occur as a variety of intertrigo mainly confined to the deep folds or involve the pubic area and labia majora. The scales are soft, greasy and lightly attached, thus differing from psoriasis. Pruritus is a variable feature but when marked the soft skin is readily damaged by scratching and moist fissures, weeping dermatitis or eczema are common sequelæ.

Mention should be made here of the other types of intertrigo. The simple type is due to friction or to irritating discharges or urine especially if glycosuria is present. Infected varieties may be caused by pus cocci, yeasts or fungi as well as the seborrhœic type just mentioned.

Lichen planus may affect the vulva as part of an extensive eruption or may be localized there. In the former instance the diagnosis rarely presents difficulty for although aggregated papules may resemble psoriasis or lichen simplex, the discrete lesions are characteristic oval or round, flat-topped, lilac-tinted papules having a shiny surface stippled with fine white striæ. When generalized the eruption is symmetrical and the papules on the flexural surfaces of the forearms are readily recognized. The lesions itch, often intensely, and may persist for many months eventually fading into brown macules or atrophic spots. Atrophy may be an early feature and involve the whole skin which is manifest most patently when hairy regions are involved and a permanent alopecia results. Besides the atrophic variety of lichen planus, bullous, hypertrophic and follicular lesions occur and the rarer manifestations of this disease provide some of the most difficult diagnostic problems of dermatology which may also baffle the expert pathologist.

Lichen sclerosus vel atrophicus is an outstanding example. Identical or very similar lesions undoubtedly occur at times with indisputable lichen planus lesions but in many cases the papules of lichen sclerosus keep their identity and neither clinically nor histologically can their relationship with lichen planus be incontrovertibly established.

The eruption of lichen sclerosus consists of irregular, polygonal, flat-topped, white papules or macules, discrete or grouped. The smooth shiny surface of each papule is speckled with minute, dark, horny plugs or with the dilated follicular orifices left by such plugs. Later atrophic changes produce a thin integument resembling parchment or wrinkled tissue paper. Lichen sclerosus is said to be six times more common in women than in men and usually develops in the later decades, but may begin in childhood. The sites affected are the upper parts of the trunk, the neck, axillæ, and forearms, and the vulva. In 20 out of 46 cases mentioned by Ormsby and Montgomery (1943) the vulva was involved with other parts of the body, and in 6 cases the vulva

and anus only were affected. In this series no lesions were observed on the buccal mucosa. Pruritus is slight, and only occurs in about half the cases. The histology shows relative and absolute hyperkeratosis with horny plugging of the hair follicles, atrophy of the epidermis with flattening of the capillary processes, œdema of the upper part of the dermis, and an infiltrate beneath. No obliteration of deep vessels is seen as in morphœa and kraurosis.

On the vulva the papules may be arranged in linear or circinate patterns and are sometimes aggregated to form larger nodules, especially on the external surfaces of the labia majora, in the genitocrural flexures, on the perineum or about the anus. Larger confluent lesions may present a smooth parchment-like area or a rough, horny patch and narrow horny bands may be seen on the internal surfaces of the vulva, extending from the mons veneris to the anus, sometimes invading the vagina. The course is usually very chronic, and the ultimate atrophy causes shrinking of the labia minora and folds of the clitoris. When the orifice of the vagina or the anus is involved considerable contraction is the result. Red areas and telangiectases are often seen with the atrophic areas. There is little doubt that in the late stages lichen sclerosus gives a clinical picture indistinguishable from that described as kraurosis.

In the differential diagnosis of white patches on the skin we have to consider morphœa or localized scleroderma, which may produce lesions very similar to the atrophic patches of lichen sclerosus. Sometimes the lesions arise as smooth, waxlike plaques in the skin, or they may follow an erythematous reaction, and some red or lilac colour may persist round a white lesion.

Vitiligo or leukodermia also produces white depigmented areas in the skin, but the absence of atrophy indicates the diagnosis.

Let us now consider lesions of the mucous membranes. Lichen planus commonly affects the mucous membrane of the mouth and the vulva and it may occur independently in either situation. The characteristic lesions consist of opaque, white, greyish or silvery flecks, or streaks or patches, and occasionally small flat-topped, ivory-coloured papules may be seen. Patients are usually unaware of the existence of these lesions.

The term leukoplakia has been applied to a number of white lesions of the mucous membranes. Schwimmer (1877) described two types, the first showing greyish or silvery-white streaks and patches and a smooth shiny surface, which corresponds to the lesions of lichen planus and lupus erythematosus, and very rarely of psoriasis of the mucous membrane, and it is obviously less confusing, if there is any clinical evidence of these diseases elsewhere, to label the mucous membrane lesions according to the disease of which they form a recognized part.

The second type of leukoplakia described by Schwimmer consists of whitish, thickened, and rough horny patches which represent hyperplasia of the epithelium, and perhaps a better name for this condition is leukokeratosis. It is recognized that this condition is precancerous, and its association with senile keratosis has been observed. Leukokeratosis of the buccal cavity is known to be related to local irritation and chronic infection, and it is therefore not surprising that the condition should occur with greater frequency on the mucous surfaces of the vulva in chronic pruritus, whatever the cause of the pruritus may be. A chronic vulvitis is bound to occur with scratching, not only as the result of trauma, but by the inevitable infection of minute excoriations and in elderly patients who are probably predisposed to epithelial hyperplasia one would expect leuko-keratosis to develop. Savill (1940) regards this as the probable explanation of leuko-plakic vulvitis, as described by Bonney (1938). Hunt (1943) considers that many of the cases described as leukoplakic vulvitis are late manifestations of lichen planus or a clinical variation of it, lichen sclerosus. Bonney (1938) lays stress upon the precarcino-matous states, amongst which leukoplakic vulvitis is one of the most impressive, and therefore it would appear that the condition he describes as leukoplakic vulvitis is leuko-keratosis, but some of his clinical and histological observations certainly apply to lichen planus and lichen sclerosus.

It should be remembered that thickened, white patches occur on mucous surfaces as a result of yeast infection.

Kraurosis vulvæ as described by Breisky (1885) is essentially a condition of cutaneous atrophy of the pudenda with shrinking, and from a dermatological point of view one would regard the condition as a syndrome which might follow any atrophic skin disease, such as lichen planus or lichen sclerosus, as well as senile changes. Whether there is a clinical entity for which the name should properly be reserved, as suggested by Bonney, I am quite unable to determine from the literature, and one's personal experience is too small to justify a criticism of his thesis.

I am indebted to the monograph on "Diseases Affecting the Vulva", by Dr. Elizabeth Hunt, and to papers by Dr. A. Savill.

ities which do not allow the most expert pathologist to make a diagnosis with any more confidence than his clinical confrère.

The first lesion to consider is lichen simplex, which is usually regarded as a neurogenic lesion resulting from prolonged scratching. Thus, every case of pruritus vulvæ is bound to be complicated by some of the features of lichenification which is made manifest by a general thickening of the skin, presumably because repeated trauma maintains a chronic inflammatory condition, and the friction and the dilatation of vessels account for hypertrophy of the epidermis. Histologically this is shown by acanthosis, enlarged papillæ produced by down-growths of the epidermis, and various degrees of œdema and infiltration of the papillæ and the underlying dermis. Hyperkeratosis may be marked. Clinically, lichen simplex is recognized as a well-defined area of dull red or brownish red colour with marked exaggeration of the normal grooves of the skin, which divide the thickened area into lozenge-shaped, flat papules. When the skin surface is moist, the increased horny scale is macerated and whitened and the appearances are indistinguishable from those described by Bonney in 1938, which he termed lepidosis vulvæ.

Chronic irritation of the skin by external factors such as irritating discharges and recurrent mild infections may produce very similar appearances, and they are the secondary features of many cases of chronic dermatitis and eczema, very familiar to dermatologists.

Psoriasis of the vulva may closely simulate lichen simplex and since pruritus is common at this site some degree of lichenification is usually superimposed upon the psoriasis. However, the eruption precedes the symptoms, the colour is a brighter red and the skin surface shiny, with a thin, closely adherent scale which shows silvery lines when lightly scratched. The mons veneris is often first affected and the lesion then extends over the external surfaces of the labia majora to the perineum and anal region, and may involve the whole gluteal cleft. Psoriasis rarely affects the mucous surfaces but instances have been reported: mostly buccal lesions similar to those about to be described in lichen planus. The diagnosis may be facilitated if characteristic lesions are found on other parts of the body and thimble-like pittings of the nails and subungual hyperkeratosis may give helpful clues.

Seborrhœic dermatitis somewhat resembles the flexural type of psoriasis and may occur as a variety of intertrigo mainly confined to the deep folds or involve the pubic area and labia majora. The scales are soft, greasy and lightly attached, thus differing from psoriasis. Pruritus is a variable feature but when marked the soft skin is readily damaged by scratching and moist fissures, weeping dermatitis or eczema are common sequelæ.

Mention should be made here of the other types of intertrigo. The simple type is due to friction or to irritating discharges or urine especially if glycosuria is present. Infected varieties may be caused by pus cocci, yeasts or fungi as well as the seborrhœic type just mentioned.

Lichen planus may affect the vulva as part of an extensive eruption or may be localized there. In the former instance the diagnosis rarely presents difficulty for although aggregated papules may resemble psoriasis or lichen simplex, the discrete lesions are characteristic oval or round, flat-topped, lilac-tinted papules having a shiny surface stippled with fine white striæ. When generalized the eruption is symmetrical and the papules on the flexural surfaces of the forearms are readily recognized. The lesions itch, often intensely, and may persist for many months eventually fading into brown macules or atrophic spots. Atrophy may be an early feature and involve the whole skin which is manifest most patently when hairy regions are involved and a permanent alopecia results. Besides the atrophic variety of lichen planus, bullous, hypertrophic and follicular lesions occur and the rarer manifestations of this disease provide some of the most difficult diagnostic problems of dermatology which may also baffle the expert pathologist.

Lichen sclerosus vel atrophicus is an outstanding example. Identical or very similar lesions undoubtedly occur at times with indisputable lichen planus lesions but in many cases the papules of lichen sclerosus keep their identity and neither clinically nor histologically can their relationship with lichen planus be incontrovertibly established.

The eruption of lichen sclerosus consists of irregular, polygonal, flat-topped, white papules or macules, discrete or grouped. The smooth shiny surface of each papule is speckled with minute, dark, horny plugs or with the dilated follicular orifices left by such plugs. Later atrophic changes produce a thin integument resembling parchment or wrinkled tissue paper. Lichen sclerosus is said to be six times more common in women than in men and usually develops in the later decades, but may begin in childhood. The sites affected are the upper parts of the trunk, the neck, axillæ, and forearms, and the vulva. In 20 out of 46 cases mentioned by Ormsby and Montgomery (1943) the vulva was involved with other parts of the body, and in 6 cases the vulva

[*April* 21, 1944]

A Solid Ovarian Teratoma.—V. B. Green-Armytage, F.R.C.O.G., and R. G. L. Waller, M.R.C.S., L.R.C.P.

Miss P. B., aged 20, was sent by Dr. MacArthur to the West London Hospital on February 11, 1944, complaining of an abdominal tumour the size of a seven months' pregnancy and two months' amenorrhœa.

The breasts were active but examination, auscultation, X-rays and a negative Aschheim-Zondek test eliminated pregnancy. The mottled appearance of the radiograph together with the ascites present suggested the preoperative diagnosis of teratoma.

Left ovariotomy was performed on March 23, 1944, the tumour being the size of a full-size rugby football after removal. The right ovary and uterus were conserved. There were no adhesions.

Gross and histological appearances (R. G. L. W.).—The tumour which weighs 1,320 g. (about 3 lb.) is contained within a thick-walled capsule and has a variegated, lobulated appearance; small areas of cystic degeneration are present. The gross appearances correspond with those of a solid ovarian teratoma. Similar tumours weighing up to 25 kg. (about 55 lb.) are recorded.

In the tumour the following types of tissue were observed: Squamous epithelium and keratin; hair follicles and sebaceous glands; fat and fibrous tissue; muscle bundles; cartilage and bone; blood-vessels and lymphoid tissue; salivary gland tissue; secreting glandular tissue resembling mammary gland: tall mucus-secreting epithelium resembling large intestine; tall ciliated columnar epithelium resembling bronchial mucosa; nervous tissue resembling brain tissue; other epithelial tissue unidentified, some of which resembles Fallopian tube.

Pathologists like Bland-Sutton, Ewing, Boyd, Beattie and Dickson state that these rarest of all ovarian tumours are malignant from the start and that they grow with extreme rapidity producing metastases of embryonic tissue that are sarcomatous in type.

Gynæcologists are, however, divided in their opinion as to the correct surgical procedure, for whereas Frank records a mortality of 88·8% within a year of operation, Curtis of Chicago states that 27% recover completely without hazard. Wilfred Shaw considers that at least 20% are innocent.

Hartman, Fraenkel, Williams and Chipman consider that if the patient is young, the ovarian capsule intact and the other ovary healthy, conservative surgery should be advocated; whereas Graves, Frank and Bonney advise complete extirpation of the uterus and both ovaries whatever the age and condition present.

Judging by the long experience of one of us (V. B. G.-A.) and that of H. R. Spencer, these cases are very rare. In the first case operated upon by me (V. B. G.-A.), I removed uterus and both ovaries and the patient succumbed from pulmonary metastases in seven months' time. This present case has not been watched long enough to assess the result of conservative measures.

Postscript (May 12, 1944).—Patient's condition is satisfactory.

A SUMMARY OF THE PATHOLOGY OF SOLID OVARIAN TERATOMA

The cystic dermoid and solid teratoma of the ovary together appear to constitute about 10% of all ovarian tumours; the solid teratomas being very much the less frequent. Cystic dermoids and solid teratomas probably have an identical origin and appear to represent the extremes of a series of tumours arising from a common source. The cystic dermoid is initially benign and may rarely become carcinomatous; the solid teratoma is generally regarded as malignant from the start; the intermediate types are less or more liable to be malignant according to their position in the series.

REFERENCES

BONNEY, V. (1938) *Proc. R. Soc. Med.*, **31**, 1057.
HUNT, E. (1943) Diseases of the Vulva. 2nd Ed., London.
ORMSBY, O. S., and MONTGOMERY, H. (1943) Diseases of the Skin. Philadelphia.
SAVILL, A. (1940) *Brit. J. Derm.*, **52**, 321.
Many other references are included in the second and fourth references.

Dr. Agnes Savill (London) said she had been fortunate, during the last war, to be near Paris, where she saw much electrotherapy for women's diseases; after that she had seen the pioneer work of Cumberbatch with diathermy for pelvic conditions. Many vulvar conditions had been sent to her by gynæcologists, usually wrongly named leukoplakia. True leukoplakia was very rare: raised white patches which later became malignant. The majority of vulvar cases could be grouped under three headings: (1) Lichenification: admirably illustrated by Victor Bonney in *Proceedings*, 1938, **31**, 1057, under the title of "Lepidosis". This occurred at any age, thick, grooved, dry (unless complicated), due to scratching, lasting long, not malignant. (2) Dermatitis (eczema); swollen, weeping, crusted, with horny layer sodden and white, which gave rise to the wrong label of leukoplakia. Usually associated with vulvitis, and when secondarily infected, extending to all adjacent skin. This was the condition often called "Leukoplakic Vulvitis". In its later stage, subepithelial infection led to contraction, atrophy, and hence to confusion with kraurosis. It should be described as the *late* or *contracted stage of leukoplakic vulvitis*. (3) True kraurosis was seen in elderly or castrated younger women. This was an atrophic condition; Darier's classical description is advocated also by Hamilton Montgomery of the Mayo Clinic, who has carried out histological research on all these vulvar diseases. Dr. Savill believed that the caruncle, the tenderness on passing water, the red, often purpuric patches so often seen with true kraurosis, are due to recurring complications—vulvitis, urethritis, and senile vaginitis. *B. coli* infection is a frequent cause of these recurrences of active symptoms with kraurosis; treatment with urethral ionization relieves most patients. The contraction of both the later stages of "leukoplakic vulvitis" and of kraurosis can be immensely and rapidly relieved by pelvic diathermy. Full details of cases observed over a long term of years were described in her papers—*Brit. J. Derm.* (1940), **52**, 321 and 353; and *J. Obstet. and Gynæc.*, (1942), **49**, 310.

Mr. Stanley W. Wright: Little has been said regarding the treatment of these cases of leukoplakia. In 1942 Shute of Toronto published a paper (*J. Obstet. Gynæc.*, **49**, 534) in which he pointed out that there were two types, judged by their response to treatment. One group responded to œstrogenic therapy, the other was aggravated by œstrogens and responded to progesterone.

A case was described which had the clinical appearance of leukoplakia, in which there coexisted non-ovular bleeding, a diagnosis supported by the histology of the endometrium. As this appeared to contra-indicate œstrogenic therapy, progesterone was given: 5·0 mg. twice weekly for two weeks; 5 mg. weekly for a further four weeks. Immediate response of the leukoplakic condition was noticed—all irritation disappeared in five days, and within two weeks the condition of the vulval skin appeared almost normal.

POSTSCRIPT (14.6.44): The patient remains well on a maintenance dose of 2·0 mg. progesterone every other week, although the menses remain heavy. It is interesting to speculate whether hysterectomy for the menorrhagia will result in permanent cure of leukoplakia.

Dr. Janet Bottomley: Many patients complaining of chronic lesions of the vulva are seen in the gynæcological out-patient department, but leukoplakia as described by Mr. Bonney is rarely found. The majority of cases show one or other of the conditions described by the dermatologists. It is most suitable that these patients should be treated in co-operation with the skin department.

Kraurosis responds rapidly to œstrin, which I give in the form of pessaries. Leukoplakia is resistant to treatment by conservative means.

Dr. H. C. Semon thought the condition so ably described and illustrated by Bonney and designated leukoplakia vulvæ must be very uncommon in dermatological practice, in which pruritus vulvæ, due to a variety of causes, abounded. He could not recollect seeing more than one or two cases, clinically similar to those described, in over thirty years of hospital and private work. The other entity, kraurosis vulvæ, appeared to be equally rare.

In neither of them, considering the underlying histological features, in which atrophy and eventual fibrosis seemed prominent, would he use X-rays except as a very temporary measure, and in the smallest doses, as an antipruritic treatment. He agreed that much damage had been done by radiotherapy in such cases by overdosage in the past, and dermatologists generally were very much alive to the risks involved, and differentiated their cases accordingly. He thought the symptoms of radiodermatitis described by a previous speaker, in which hypertrophic changes seemed predominant, were possibly due to some other cause—as atrophy and telangiectases with shifting of pigment, were more characteristic of radiodermatitis.

passage into the bladder was situated at the posterior part of the mass (*see* fig.). By firm, sustained pressure the mass was replaced. There was an obvious tendency to recurrence, and a catheter was therefore inserted into the bladder and secured in position with the hope that the constant pressure would prevent a renewed protrusion of the mucosa. This treatment was only partly successful; by next day, in spite of immobilizing the child as much as possible, the catheter became dislodged and the prolapse returned as before.

Two days later the child was again anæsthetized. Four fine catgut stitches were inserted, flush with the fossa navicularis, passing from the outside to the urethra, and from urethra back to the starting point. The sutures were then tied, and the redundant mucosa excised. A catheter was not inserted. The child made an uninterrupted recovery, and at no time had she any difficulty with micturition. She has been seen again recently (18.4.44), and it is not now possible to detect any abnormality. Micturition is normal. On questioning, the mother states that the child has some "urgency" but never wets herself, nor does she want to void urine unusually often.

Prolapse of the mucous membrane of the urethra is a rare condition and I am not aware of any previous record of its occurrence in a child. It is probably associated with an unusually wide urethra; this seemed to be so in the case described.

It would be interesting to know how much mucosa can be drawn down and excised without interference with the bladder function. In this case the excision caused no appreciable ill-effect.

Endometriosis of the Umbilicus.—J. CHASSAR MOIR, F.R.C.S.Ed.

Miss L., aged 47 years, complained that for three or four years she had had a slight discharge of blood from the umbilicus with each menstruation. This was accompanied by pain in that area. Menstruation was normal and not accompanied by any unusual lower abdominal pain.

On inspection, the umbilicus was found to be rather deep, and at the bottom there was a small brownish projection. Gynæcological examination suggested some thickenings

Endometriosis of umbilicus.
The skin and endometrial glands are seen in close approximation.

The Common Origin of This Series of Tumours

The blastomere theory. (*Marchand Bonnet*).—These tumours are considered to arise from blastomeres detached from the ovum during its primary segmentation; the blastomere may then, theoretically, become embedded in any part of the developing embryo and give rise in later life to a teratoma. Thus a person may be born with a teratomatous focus already present. On this theory it is difficult to understand why these tumours should arise more commonly in the ovary than elsewhere.

The sex cell theory (*Ewing*).—These tumours are regarded as arising, not in the embryonic stage, but during the period of functional activity of the ovary of the patient and most commonly in young adults at about the age of 20 years. The theory postulates an origin from an ovum which though unfertilized nevertheless undergoes spontaneous growth in an imperfect and abnormal manner. According to this theory therefore the teratomatous focus is not present at birth.

The solid ovarian teratomas are of complex structure in which elements of all organs have at one time or another been identified. These elements of the various tissues of the body are mixed indiscriminately without any attempt at formation of complete organs. The degree of malignancy in the series of tumours appears to be dependent upon the extent of differentiation or absence of differentiation into completed organs.

Owing to the absence of differentiation, this present tumour must be regarded as malignant and liable to give rise to metastases of a sarcomatous or undifferentiated embryonal type via the blood-stream, chiefly in the lungs and liver.

Perforation of the capsule does not appear to have occurred in this case, so that direct extension or implants within the pelvic or abdominal cavities are unlikely.

Prolapse of Urethra in a Child of 6 years.—J. CHASSAR MOIR, F.R.C.S.Ed.

G. G., a healthy child of 6 years, suddenly started to bleed from the vulva. The mother saw what she took to be a large blood-clot at the entrance to the vagina. There was no previous history of bleeding or of bladder symptoms.

Next day (19.1.43) the child was sent to hospital. She complained of soreness, and there was still a slight loss of blood. A dark red, velvety mass nearly an inch in diameter, bulged through between the labia and obscured all the structures in that region. My house-surgeon—an experienced man—reported that he imagined that the child must be suffering from some rapidly growing, fungating sarcoma. An X-ray examination did not show any foreign body in the bladder.

Under anæsthesia fuller examination was possible, and it became obvious that the condition was an extensive prolapse of the mucous membrane of the urethra. The
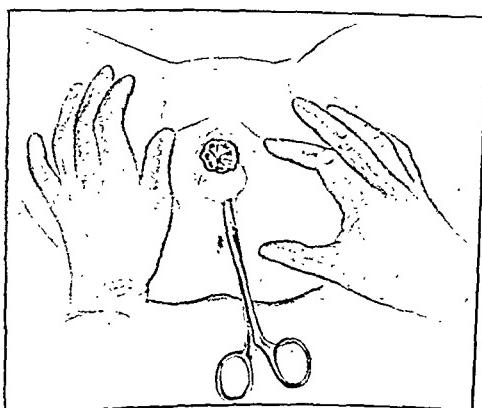
Prolapse of the urethra in a child aged 6.

passage into the bladder was situated at the posterior part of the mass (*see* fig.). By firm, sustained pressure the mass was replaced. There was an obvious tendency to recurrence, and a catheter was therefore inserted into the bladder and secured in position with the hope that the constant pressure would prevent a renewed protrusion of the mucosa. This treatment was only partly successful; by next day, in spite of immobilizing the child as much as possible, the catheter became dislodged and the prolapse returned as before.

Two days later the child was again anæsthetized. Four fine catgut stitches were inserted, flush with the fossa navicularis, passing from the outside to the urethra, and from urethra back to the starting point. The sutures were then tied, and the redundant mucosa excised. A catheter was not inserted. The child made an uninterrupted recovery, and at no time had she any difficulty with micturition. She has been seen again recently (18.4.44), and it is not now possible to detect any abnormality. Micturition is normal. On questioning, the mother states that the child has some "urgency" but never wets herself, nor does she want to void urine unusually often.

Prolapse of the mucous membrane of the urethra is a rare condition and I am not aware of any previous record of its occurrence in a child. It is probably associated with an unusually wide urethra; this seemed to be so in the case described.

It would be interesting to know how much mucosa can be drawn down and excised without interference with the bladder function. In this case the excision caused no appreciable ill-effect.

Endometriosis of the Umbilicus.—J. Chassar Moir, F.R.C.S.Ed.

Miss L., aged 47 years, complained that for three or four years she had had a slight discharge of blood from the umbilicus with each menstruation. This was accompanied by pain in that area. Menstruation was normal and not accompanied by any unusual lower abdominal pain.

On inspection, the umbilicus was found to be rather deep, and at the bottom there was a small brownish projection. Gynæcological examination suggested some thickenings

Endometriosis of umbilicus.
The skin and endometrial glands are seen in close approximation.

in the pelvis at the sides of the uterus. The patient was given instruction in the regular cleansing of the deep umbilicus, and told to report again at a later date. This she did; the symptoms were as before and she was therefore admitted to hospital.

At operation the whole umbilical area was carefully resected; it was now obvious that there was an abnormal thickening of the region, but the inner or peritoneal surface of the umbilicus was quite smooth. An opportunity now presented to examine the pelvic organs, and it was found that they were involved in an extensive endometriosis with numerous areas of tarry blood cysts. There did not appear to be any communication between the pelvic endometriosis and the umbilicus. As the patient was already at the menopausal age, and as there were no symptoms relating to the pelvic organs, further operation was not thought justifiable and the abdomen was accordingly closed.

The patient made a good recovery and when seen six months later was in excellent health. Histological examination of the umbilicus showed numerous gland areas indistinguishable from uterine mucosa in the proliferative phase (*see* fig.). Two and a half years later the patient reports that she is in good health, save for obstinate constipation, and is free from abdominal pain.

Novak states that some forty cases of endometriosis of the umbilicus have been recorded. Vartan (1937) has recently recorded two further cases in one of which there was a monthly discharge of blood. An umbilical endometriosis that not only causes pain and swelling but bleeds regularly each month is extremely rare and justifies the record now presented.

Reference.—VARTAN, C. K. (1937) *J. Obstet. Gynæc.*, 44, 715.

Inversion of Rectum Through Vagina.—J. CHASSAR MOIR, F.R.C.S.Ed.

Mrs. F. M., aged 73, suffered from a large prolapse of the uterus for many years. In 1938 she had a Mayo-Ward type operation performed by a very competent gynæcologist. While in hospital her convalescence was satisfactory. The patient stated that she was later examined by a junior house-surgeon who did not heed her complaint that all was not well. The prolapse, according to the patient, soon returned, but dissatisfied, and supposing that her old complaint had returned, she did not seek further advice.

Five years later this patient came to the Oxford area and was sent to me by her own doctor who correctly diagnosed that the prolapse was a rectal inversion. On examination, a mass of congested rectal mucosa was seen to project a full 5 in. beyond the vulva. On passing a finger into the anal canal an opening could be felt half-way up

Inversion of rectum through vagina.

the posterior vaginal wall. The finger could be hooked through this opening to present in the vagina alongside the rectal mass. The patient stated that the mass sometimes disappeared on lying down. Fæces were passed sometimes by the natural passage, and sometimes involuntarily by the vaginal route. The patient was admitted to hospital and the mass replaced by manipulation; she was then kept in bed for a few days to allow the congestion to subside.

Later, under anæsthesia, a further examination was made and photographs secured; these unfortunately do not give an adequate idea of the size of the mass as it was when first seen (*see* fig.). The recto-vaginal opening was found to measure about 1½ in. long by 1 in. wide. The mucosa was detached round the edge of the opening by sharp dissection, and closed by a fine catgut inverting stitch. The remainder of the opening was closed by an adaptation of the classical method of repairing vesico-vaginal fistulæ with which I have been well pleased: the edges were paired till free bleeding took place and the whole area "saucerized"; eight silver wire sutures were then used to bring the broad edges together. Finally, the anus was thoroughly stretched and a 1 in. flatus tube inserted and stitched in position; this was done as an alternative to colostomy.

The patient made a perfect recovery and was discharged after three weeks. She has remained in good health since (eleven months).

The exact mechanics of the prolapse are uncertain. It is probable that the posterior rectal wall protruded through the fistula. Alternatively, the mucosa alone protruded; it is well known that great mobility of the rectal mucosa on the submucous layer is possible.

Brief Clinical Notes on Two Cases of Retroperitoneal Schwannoma.—JOHN STALLWORTHY, F.R.C.S.

Tumours of nerve tissue origin are seldom found in either the abdomen or the pelvis. Robert Meyer in an article published in the *Archives of Pathology*, November 1943, summarized the present views on these tumours, and suggested a simplified classification of them. His article includes a good description of the nerve sheath blastoma, neurinoma or schwannoma. Stout, Laidlaw and Haagensen collected 246 cases of schwannomata and in their series found that only four occurred in the abdomen and three in the pelvis. ("Tumors of the Nervous System", Association for Research in Nervous and Mental Disease, Vol. XVI, New York, 1937.)

The clinical characteristics of these tumours are that they produce symptoms by pressure effects, by the size they sometimes reach, or by constitutional reactions secondary to degenerative changes. For the most part they are single tumours, not malignant, and if adequately removed do not recur. In this respect they should be differentiated from the neurofibroma of von Recklinghausen's disease. Common sites for their occurrence are in the nasopharynx and the skin of the upper extremities. They have not been described on the feet, in the rectum or in the urinary system.

Histologically the picture is one of capricious degeneration as a result of which the tumour tends to be divided into two zones, a dense zone in which there are aggregations of nuclei in a palisade pattern, and a loose zone with considerable intercellular œdema. The tumour is vascular and a characteristic feature is that the small vessels are surrounded by prominent collars of collagenous deposits.

CASE I.—Mrs. Y., para 4, aged 72. She was an active, alert woman who, living 5 miles from the nearest large town, used to walk in there once a week to supervise her own shopping. Over a period of two or three months she found that she was rapidly losing weight, becoming lethargic, and experiencing considerable pelvic and rectal discomfort. Examination revealed a firm, well-defined, tumour which was not tender, filling the pelvis and pressing on the rectum. There was no ascites, and there were no urinary symptoms. The diagnosis of an impacted degenerating fibroid was made and exploration advised. At operation on 8.5.43 a tumour the size of a fœtal head was found growing from the hollow of the sacrum. The rectum was displaced to the right and a small post-menopausal uterus was pushed well forwards behind the symphysis. The peritoneum over the tumour was divided and without any difficulty the mass was shelled out from a relatively non-vascular bed. On section in the theatre it was found that the central portion of the tumour was completely degenerated and cystic with xanthomatous

in the pelvis at the sides of the uterus. The patient was given instruction in the regular cleansing of the deep umbilicus, and told to report again at a later date. This she did; the symptoms were as before and she was therefore admitted to hospital.

At operation the whole umbilical area was carefully resected; it was now obvious that there was an abnormal thickening of the region, but the inner or peritoneal surface of the umbilicus was quite smooth. An opportunity now presented to examine the pelvic organs, and it was found that they were involved in an extensive endometriosis with numerous areas of tarry blood cysts. There did not appear to be any communication between the pelvic endometriosis and the umbilicus. As the patient was already at the menopausal age, and as there were no symptoms relating to the pelvic organs, further operation was not thought justifiable and the abdomen was accordingly closed.

The patient made a good recovery and when seen six months later was in excellent health. Histological examination of the umbilicus showed numerous gland areas indistinguishable from uterine mucosa in the proliferative phase (*see* fig.). Two and a half years later the patient reports that she is in good health, save for obstinate constipation, and is free from abdominal pain.

Novak states that some forty cases of endometriosis of the umbilicus have been recorded. Vartan (1937) has recently recorded two further cases in one of which there was a monthly discharge of blood. An umbilical endometriosis that not only causes pain and swelling but bleeds regularly each month is extremely rare and justifies the record now presented.

Reference.—VARTAN, C. K. (1937) *J. Obstet. Gynæc.*, 44, 715.

Inversion of Rectum Through Vagina.—J. CHASSAR MOIR, F.R.C.S.Ed.

Mrs. F. M., aged 73, suffered from a large prolapse of the uterus for many years. In 1938 she had a Mayo-Ward type operation performed by a very competent gynæcologist. While in hospital her convalescence was satisfactory. The patient stated that she was later examined by a junior house-surgeon who did not heed her complaint that all was not well. The prolapse, according to the patient, soon returned, but dissatisfied, and supposing that her old complaint had returned, she did not seek further advice.

Five years later this patient came to the Oxford area and was sent to me by her own doctor who correctly diagnosed that the prolapse was a rectal inversion. On examination, a mass of congested rectal mucosa was seen to project a full 5 in. beyond the vulva. On passing a finger into the anal canal an opening could be felt half-way up

Inversion of rectum through vagina.

Section of Comparative Medicine

President—J. T. EDWARDS, M.R.C.V.S.

[*February* 16, 1944]

DISCUSSION ON THE LIMITATIONS AND USES OF THE COMPARATIVE METHOD IN MEDICINE

III. Nutrition and Endocrinology

(*For Discussion No. II see* PROCEEDINGS, 1944, *February*, 37, 121)

Dr. H. H. Green : In considering nutrition and endocrinology in relation to disease of the larger domesticated animals it is not always easy to decide whether a given syndrome is due to specific nutritional deficiency, or primarily to endocrine dysfunction, or to faulty operation of other physiological mechanisms for utilization of nutrients.

A quarter of a century ago, before the nutritional relationships between calcium, phosphorus, vitamin D and sunlight were clearly recognized, the so-called "stiff-sickness" of grazing cows in South Africa was attributed to plant poisoning and referred to as "crotalism". From 1918 onwards the true relationships became recognized and to-day the position is clear. When the syndrome of rickets or osteomalacia occurs in pigs or poultry intensively reared on cereal products rich in phosphorus but low in calcium, its ætiology is the same as that of the human subject—combined deficiency of vitamin D and calcium. In grazing animals it does not occur in this country at all, since so much of their life is spent out of doors and the leafy parts of plants are rich in calcium. But in many parts of the world the soil is so deficient in phosphorus that although young grass still contains the moderate amounts prerequisite for its own growth, the translocation of the element from leaf to seed, leaves the residual vegetative parts deficient for cattle grazing under ranching conditions. They then develop aphosphorosis, characterized by depraved appetite, stunted growth, reduced fertility, and in extreme cases by the osteodystrophic changes histologically recognizable as osteomalacia. In the same areas sheep may escape the grosser manifestations of aphosphorosis, a difference attributable to the different habits of prehension of the two species of ruminant. The bovine consumes tufts of older, stemmy grass, the sheep nibbles closer to the ground and selects younger, leafier vegetation, richer in phosphorus.

Another disorder associated with calcium and phosphorus metabolism, which is of interest from the point of view of comparative medicine, is *osteodystrophia fibrosa* of the horse. The real cause is improper balance between calcium and phosphorus in the diet. If the ratio, expressed as the oxides CaO and P_2O_5, as in agricultural usage, exceeds 1:3 equines will gradually develop osteofibrosis, a disease histologically not unlike von Recklinghausen's disease in man. Human dietaries commonly show a calcium phosphorus ratio as wide as that occasioning osteitis fibrosa in the horse but the corresponding disease does not seem to be shown in man unless associated with tumours of the parathyroid glands. The reason for the apparent involvement of endocrine function in one species and not the other is not clear.

Hypomagnesæmia.—With regard to association of endocrine function with mineral metabolism, there are several diseases in animals apparently having no parallel in human

and hæmorrhagic areas suggesting the presence of sarcomatous degeneration. Histologically the tumour showed the characteristic features of a schwannoma. The patient made a rapid recovery, regained her health, and a year later is active and well.

CASE II.—Miss A., a nullipara of 42, complained of progressive swelling of her abdomen over a period of two years. Frequency of micturition and menstrual irregularity characterized by oligomenorrhœa and infrequent periods had been present for one year. The patient looked very well but the abdomen in contour and size resembled that of a woman who was 28 weeks' pregnant. There was a fixed abdomino-pelvic tumour, tensely cystic, with a loop of bowel running obliquely across above the umbilicus. There was no ascites. The diagnosis of an ovarian cyst was made, and at operation on 3.9.43 the tumour was removed. It was retroperitoneal and could be approached only after the transverse and descending colon had been mobilized. Removal of this tumour was most difficult. The ureter was displayed in the whole of its abdominal course, and even when this was done the tumour was still firmly fixed apparently to the vertebral column at the level of the bifurcation of the aorta. When a plane of separation was found the base from which the tumour had sprung was non-vascular. Section showed that this tumour was also degenerated with large cystic areas, and on section it presented the characteristic features already described.

This patient also made a rapid recovery and six months later was perfectly well.

inevitable. This is far from representing the whole story, however, since hypocalcæmia occasionally occurs in the cow well in advance of lactation. In the case of sheep pre-parturient hypocalcæmia, occurring about ten days before lambing, is quite common. The primary disturbance is obviously endocrine, and not nutritional shortage of calcium. Although it is possible that the statistical incidence of milk fever may be somewhat less on high calcium intake than on low, the disorder occurs in cows receiving large mineral supplements all the year round. On the other hand it is almost unknown in uncivilized cows under ranching conditions, even where the pastures are low in calcium.

Chronic hypocalcæmias are also known in ruminants but where the fall in calcium is sudden all that is required to effect a cure is to elevate artificially the level of blood calcium for the brief period necessary to allow the animal to recapture control of its own physiological equilibrating mechanism. The response to an injection of calcium boro-gluconate is often spectacular and a comatose cow may be on her feet again in half an hour. The subsequent fall of the induced high calcium level is very rapid but instead of continuing to the pre-injection point it is arrested near the normal level and recovery is effected without regard to diet, despite the continuous subsequent lactation drain.

Post-parturient hypocalcæmia is also known in the sow, the mare and the bitch, and it is therefore of interest to note that it appears to be entirely unknown in the human female.

Ketosis.—Amongst other disorders of ruminants in which the nutritional factor may at first sight appear to be dominant but which on closer inspection appears to be conditioned by defective endocrine function, are the pregnancy toxæmia of ewes and the post-parturient hypoglycæmic acetonæmia of cows. The former is confined, for all practical purposes, to ewes carrying more than one fœtus, occurs about a month before lambing, and is most commonly precipitated by sudden interruption of nutrition occasioned by adverse weather conditions. It can be experimentally produced by cutting down food supplies in late pregnancy but not in early pregnancy. The most pronounced feature of the blood picture is acetonæmia, with figures up to thirty times the normal value, and hypoglycæmia is a common concomitant. The temptation is therefore to regard the disease as wholly nutritional, to explain the acetonæmia as due to combustion of body fat in absence of adequate carbohydrate and to explain the twin lamb incidence by saying that two fœtuses make higher demands than one on blood sugar. But once the disorder is established, response to feeding abundant carbohydrate or to glucose injections is very poor and mortality remains high. In some cases the interruption of nutrition can be shown to have been very brief, and in others no interruption can be traced at all in fat ewes which, if caught in the early stages of the disease, respond much better to enforced exercise than they do to increased carbohydrate intake. It is difficult to escape the conviction that the primary factor in the ketosis, and in the hypoglycæmia where such is also shown, is disturbed balance of endocrine secretions, most probably of the pituitary gland; and that although malnutrition is the commonest precipitating cause it only operates in an animal in an "endocrinologically labile state". It seems at least probable that injection of selected pituitary extracts might precipitate the disorder equally well.

Preparturient ketosis of the type corresponding to pregnancy toxæmia in the ewe is rare in the cow but post-parturient hypoglycæmic ketosis, rare in the ewe, is quite common as a clinical entity in the dairy cow. Moderate acetonæmia without hypoglycæmia and with no clinical symptoms is also quite common in the stall-fed cow irrespective of stage of sexual life. This mild winter ketosis is commonest in heavy milkers fed for high production and can certainly not be attributed to shortage of exogenous carbohydrate.

The post-parturient ketosis manifested clinically by fall in milk yield and loss of condition is associated with inappetence, but "dyspepsia" is an effect rather than a cause of the disorder. The cow may be feeding well for ten days after calving and then develop acetonæmia despite the endeavours of the stockman to induce it to eat as much grain food as possible. In some cases persistent intravenous injections of glucose at intervals of a few days may temporarily abolish the ketosis by forcibly abolishing the hypoglycæmia and so allow the animal to lift itself out of a metabolic vicious cycle, but the treatment is by no means certain and it seems obvious that behind the apparent disturbance of carbohydrate-fat metabolism there is a primary disturbance of endocrine function, the precise nature of which has not yet been elucidated.

Dr. S. J. Folley (*Abridged*): The purpose of this paper is to consider how far experiments on animals have led to advances in the clinical application of endocrinology and to emphasize the precautions to be observed in the application to man of the results of experiments on other species.

medicine, which on cursory inspection suggest themselves as nutritional in origin but on closer study much more strongly suggest endocrine dysfunction. Perhaps the most striking is bovine hypomagnesæmia manifested in clinical form as the so-called "grass tetany". In the human subject the level of plasma magnesium rarely if ever deviates far from the normal but in grazing cattle it may vary in downward direction throughout the year. The fall may be quite slow, an average summer value of about 2·4 mg.% dropping through autumn and winter to an early spring value of half or one-third this figure. This "seasonal hypomagnesæmia" observed on some farms and not on others, in some seasons and not in others, may occur without any obvious clinical symptoms and is only detected when periodic blood analyses are made for investigational purposes. The neuromuscular mechanisms of the animal apparently adjust themselves to the gradual change in plasma magnesium level and no hyperæsthesia is displayed. If a magnesium injection is given the temporarily elevated plasma magnesium value rapidly declines, by distribution over the tissues, and the initial subnormal value returns within twenty-four hours.

If these were the only observations one might be tempted to associate this seasonal hypomagnesæmia with variations of quantity of magnesium in the grass, or with availability for digestive absorption, and think in terms of nutritional deficiency. But the rest of the story is against any such superficial view, for a normal level of plasma magnesium may also drop quite suddenly, even to one-fifth normal within a few days. This is not uncommon in a herd of cows abruptly turned out from winter stalls to young spring grass. Within a week there may be a crop of cases of acute hypomagnesæmic tetany terminating in fatal convulsions. With rapid fall of plasma magnesium the neuromuscular mechanisms have no time to adjust themselves to the change and pronounced hyperæsthesia occurs. If a typical case of such rapidly developing "grass tetany" is treated by injection of magnesium sulphate the hyperæsthesia is corrected and the convulsions are allayed. The high artificial level of plasma magnesium of course begins to fall at once but this time, unlike the preceding case of slowly developing seasonal hypomagnesæmia, the fall does not continue to the pre-injection level but is arrested at or near the normal level. With luck the cure is permanent despite the fact that nutritional and environmental conditions remain unchanged.

In between these two extremes comes a third type of hypomagnesæmia which from the point of view of the veterinary practitioner is the most unsatisfactory form. The fall is intermediate in rate, extending over many days, even a few weeks, but not months. The time is insufficient for adaptation of neuromuscular responses and a state of latent tetany develops, from which a convulsive attack may easily be precipitated. A magnesium injection allays clinical symptoms when they appear but the fall of plasma magnesium from the high artificially induced level is no longer arrested near the normal but tends to continue to the preceding latent tetany value. From this point it may spontaneously rise again over the ensuing weeks and the practitioner may report a cure for magnesium therapy; or further acute attacks may be precipitated from the latent phase and the animal succumb to one of them.

No correlation can be traced between dietary intake of magnesium and occurrence of the disorder, and surveying the phenomena as a whole it seems reasonable to assume that the hypomagnesæmia arises from temporary dysfunction of a physiological mechanism, presumably endocrine, for maintaining the plasma magnesium at the constant level shown by most animals in health. Relatively little is known concerning the causes of the presumed dysfunction and almost nothing about the physiological mechanism itself. There is some slight evidence that the pituitary gland may be concerned. Seasonal hypomagnesæmia has also been observed in sheep but convulsive tetany is rare.

Hypocalcæmia.—Disorders of ruminants associated with hypocalcæmia are also common, the best known being "milk fever" of cows and its analogue "lambing sickness" of ewes. The blood calcium drops quite suddenly soon after parturition, commonly to half its normal value. This is usually accompanied by a fall in inorganic phosphate and rise of plasma magnesium. Normal calvings are frequently associated with a slight depression of blood calcium and phosphate, with slight elevation of magnesium, and "milk fever" might almost be regarded as a pathological exaggeration of a normal physiological phenomenon reflecting change of endocrine balance after initiation of lactation. In this case the endocrine mechanism is better known and the usual explanation given for milk fever and lambing sickness is temporary dysfunction of the parathyroids. One gallon of milk contains as much calcium as the total present in the whole circulating blood of the cow, and unless the calcium-controlling mechanism comes into operation at once, balancing the sudden demands of the udder, hypocalcæmia is

Limitations of the Comparative Method

There are two main headings concerning the limitations of the comparative method in medicine:

(1) *Species differences.*—Species differences are particularly important in the endocrine analysis of reproduction. It is not possible here to consider in detail the various types of œstrous cycle and breeding season encountered among the lower mammals but the striking species differences which have been observed in the hormone content of the anterior pituitary deserve more detailed comment. Thus horse pituitary is a very potent source of gonadotrophic activity, mainly follicle-stimulating hormone, while sheep and pig pituitary extracts contain principally luteinizing hormone. The potency of ox pituitary tissue is rather low and again luteinizing hormone predominates. Since the pituitary of the test animal is probably involved in responses to injected gonadotrophins, such functional variations between species might well explain species variations in response to gonadotrophic treatment.

Differences among species as regards the occurrence of gonadotrophins in body fluids are particularly striking. The discovery by Aschheim and Zondek of a gonadotrophin (chorionic gonadotrophin, P.U.) in the urine of pregnant women, which led to the development of a method of human pregnancy detection utilizing as test animals, the mouse, rabbit and Xenopus respectively, was the fruit of studies carried out on man. Comparative studies on other mammals, however, showed that this gonad-stimulating agent, which is mainly a luteinizing hormone, occurs normally only in the blood and urine of pregnant primates. This exclusiveness is unfortunate as regards the cow and goat, since a reliable hormonal test for early pregnancy in these domestic mammals would be invaluable. The extension of these comparative studies to the mare revealed the presence in the blood, at certain stages of pregnancy, of another gonadotrophin (P.M.S.), like P.U. believed to originate in the placenta but unlike it in that it is a powerful follicle-stimulating agent. Thus we have here an example of studies on man being profitably extended to at any rate one other form, since as a result of the discovery of P.M.S. we have a test for pregnancy in the mare and at the same time a rich and convenient source of follicle-stimulating gonadotrophin for use in human and veterinary medicine.

The vast majority of mammals do not menstruate; menstruation is restricted among mammals to the higher primates, namely the anthropoid apes, baboons and Old World monkeys, and we may expect to gain information on the endocrine control of the human menstrual cycle chiefly by studies on primates. Apes and monkeys breed relatively slowly and are expensive and thus progress in this field is less spectacular than in the case of the fundamental work leading to the isolation of the sex hormones. Experiments on apes and monkeys are making progress, nevertheless. We may take as an example the discovery of œstrogen-deprivation bleeding in the monkey and it is interesting to note that although this phenomenon must have been seen by numerous surgeons who had removed the ovaries from women its true significance was never realized by them. It must be admitted, however, that as regards the endocrine analysis and treatment of such conditions as dysmenorrhœa we are confronted by a serious limitation of the comparative method in that the monkey, unlike the human, cannot report its symptoms.

As a final example of the limitations imposed upon comparative studies by the existence of species differences, the obscurity even now surrounding the analysis of the factors controlling mammary growth may be cited. In some species, œstrogen is responsible for the growth of the mammary ducts, progesterone being required for full alveolar development. In other species, œstrogen alone seems sufficient to evoke full mammary growth. It is not yet known for certain to which category the primates belong.

(2) *Psychological and neural factors.*—Psychological or neural mechanisms play a far more important rôle in many endocrine processes in man than they do in lower animals and it is where such functions are concerned that most caution is necessary in the application to man of the results of animal experiments. The case of lactation at once comes to mind in this connexion. Even in the cow, neurological and perhaps psychological factors have an important influence on the "letting down" or release of milk from the mammary gland. How much more therefore must the control of human lactation be complicated by neural and psychological factors? Recent research has put at our disposal two methods for stimulating lactation in the cow, namely by administration of crude anterior pituitary extracts and of iodinated proteins respectively, the second of which is approaching the stage of practical application. In addition there has recently been developed a simple method of inducing copious lactation in non-pregnant, barren, bovines involving nothing more than administration of synthetic œstrogen. Nevertheless,

Advantages of the Comparative Method

(1) *Radical operative procedures.*—Operations involving total extirpation of endocrine glands, particularly such operations as hypophysectomy, pancreatectomy, parathyroidectomy and adrenalectomy are hardly possible in man, but the effects of such operations can be observed in animals. Advances in pituitary and adrenal cortex physiology have been made possible by extirpation experiments on animals. In addition, as an outstanding example, may be cited the discovery and isolation of insulin, made possible by the use of depancreatized dogs.

Unintentional experiments on man have, of course, frequently occurred in the course of surgical operations involving partial or complete removal of endocrine glands, and though such operations have often yielded valuable clues, such indications could seldom be followed up except on a comparative basis.

(2) *Economy of material.*—Probably the vast majority of endocrine experiments have been carried out on small laboratory rodents. On a body-weight basis we may take roughly 3,000 mice as equivalent to a woman. Assuming that the response is roughly proportional to body-weight, it follows that the amount of œstradiol necessary to cause development of the uterine endometrium of a mouse is about 1/3,000 of that necessary to do the same in a woman or about 1/25,000 of the amount required for a cow weighing 500 kg.

(3) *Saving of time.*—Rodents, unlike for instance cats, conveniently breed freely in cages and their œstrous cycles and gestation periods are short when measured on the human time scale. Therefore experiments on the endocrine control of growth, reproduction and lactation can be carried out on rodents with a minimum of delay. This has been of particular importance in the development of methods of bio-assay of hormones which constitutes an early and essential step in any attack upon a new field. An outstanding example is provided by the Allen-Doisy vaginal smear test for œstrogenic activity, which was one of the most important of the factors contributing to the isolation and chemical characterization of the natural œstrogens. The culmination of the advances thus set in train came with the total synthesis of one of the natural œstrogens (equilenin) and in the discovery by Dodds and his associates of the synthetic œstrogens, diethylstilbœstrol, hexœstrol and dienœstrol. One important link in the chain of events we have just been considering resulted from work on the human subject, namely, the discovery by Aschheim and Zondek of the presence of relatively large amounts of œstrogen in human pregnancy urine, a discovery which by opening up a source of œstrogens superior to any previously known, greatly facilitated their isolation and further chemical study. Even so, however, further comparative work disclosed yet a richer, though quite as convenient, source, the urine of the stallion.

Other species than rodents also have their uses in speeding the progress of endocrine research. The growth response of the capon comb to androgens is an example and Berthold's experiment on six cockerels, described ninety-six years ago, is the ancestor of numerous experiments which ultimately led to the isolation and chemical characterization of androsterone and testosterone and to the large-scale preparation of the latter from cholesterol. As in the case of the œstrogens, crystalline androgenic hormones are now available.

(4) *Long-term experiments.*—By the use of experimental animals whose normal life span is small as compared with our own, it is possible to study the effects of procedures such as deprivation of endocrine glands or administration of hormones applied over periods equivalent to say, twenty or thirty years in the human. Here again the rodent, particularly the rat and mouse, is particularly useful. Only thus was it possible to reveal the carcinogenic effect of long-term treatment with œstrogen.

(5) *Use of inbred strains of experimental animals.*—A further advantageous feature of the use of quickly breeding rodents is that highly inbred, approximately homozygous strains of animals can be quickly established, the use of which eliminates from the experiment much variability of genetic origin which might obscure the effect sought. Variability of experimental material is troublesome in, for instance, the study of milk secretion and if it were possible to breed goats as rapidly as rats, progress would be accelerated.

The use of inbred material also enables us to study the interaction of hormonal with genetic factors. The strain of recessive dwarf mice has proved useful in studies of anterior pituitary growth hormone, while the progress in studies of the relationship between sex hormones and mammary cancer resulting from the development of strains of resistant and susceptible mice may also be mentioned.

prevented and cured by nicotinic acid or amide, since used so successfully in man. "Rat pellagra", while confusing the pellagra issue, led to the identification of vitamin B₆ (pyridoxin) which is required by other species, and probably by man.

Canine blacktongue occurs naturally, but similar oral lesions are sometimes found in systemic disease of distinct ætiology, and have been noted in vitamin-A deficiency. Pig pellagra simulates necrotic enteritis, and is most easily produced at the age at which paratyphoid occurs naturally. Lesions of pig pellagra may, however, be set up in the absence of paratyphoid infection, while paratyphoid infection can be set up on a complete diet. The oral mucosa of the dog and the mucosa of the large intestine of the pig appear to be susceptible sites for local bacterial invasion, so that either a vitamin deficiency or a pathogenic infection can set up similar lesions.

The Orkney vole is related to the rat, but is herbivorous. A synthetic diet containing 10% of yeast allows optimum growth in the rat, but is inadequate for the vole. Small quantities of grass render the diet completely satisfactory for the vole. The identification of the missing factor or factors may prove important to the nutrition of the domestic herbivores.

Vitamin-B deficiencies provide examples of species, breed and individual differences. Chick and her co-workers noted that some pigs learnt to resist the deficiency in experimental pellagra either by practising coprophagy or by eating their wheat straw bedding. Slavin and myself were able to exclude these factors but noted spontaneous recovery in several instances. Hughes in California observed that some pigs overcame the deficiency by licking yeasts and moulds on the concrete floors and walls of the sty. The provision of a strictly deficient diet, the choice of suitable and presumably susceptible animals, the withdrawal of bedding and the prevention of coprophagy are not necessarily adequate if one wishes to produce deficiency symptoms in experimental stock.

Another nutritional, or partly nutritional, problem is enteric disease of the newborn. The position in man was summarized recently in the *Lancet* (1943, ii, 769-770), in which attention was drawn to Gale's work in rats. Enteritis is common in the young of domesticated mammals, and a not dissimilar syndrome appears to be responsible for severe losses in newly hatched chicks. In all these diseases, bacterial infection appears to be mixed or variable. Blakemore, Moore and myself have been able to confirm the early studies of Theobald Smith and Paul Howe regarding the importance of colostrum to the newborn calf in furnishing certain plasma globulin fractions, and have noted also its importance in supplying a rapid and available source of vitamin A. Differences in the ability of the human and of the bovine placenta to transmit substances of nutritional or immunological importance are well known, but categorical statements to the effect that the human baby is independent of colostrum do not appear to have been made on sufficient evidence. The reported greater resistance of breast-fed babies to diarrhœa and vomiting is significant, and would appear to merit investigation by biochemical techniques that were unavailable twenty years ago.

Dr. A. T. Phillipson (*Abstract*): To obtain a complete picture of the significance of any change in the level of any constituent of the blood, research must extend beyond examinations of the blood itself; the level of any constituent of the blood is an indication of the rate of exchange of that substance between its source, which is in the alimentary tract unless it is produced in the body, its place of storage, if there is one, and its rate of utilization or excretion.

The importance of comparative work is well illustrated by the study of digestion, for although the same agents may exist in all domestic species the relative importance of these agents differs considerably, thus herbivores rely largely upon bacteria as a means of digesting carbohydrate while carnivores have little need of bacterial digestion. One of the important products of bacterial fermentation of carbohydrate is a mixture of the lower fatty acids; the quantity of these acids present in the rumen and reticulum of sheep when calculated as g. acetic acid varies from 40 to 80 g. while in 3 horses we have found the quantity present in the cæcum and colon of animals weighing approximately 600 kg. to range from 250 to 350 g. These acids are also found in the large intestine of pigs and rabbits. Direct absorption of these acids occurs from the organs in which they are formed even though, in the case of the sheep, the epithelium through which they must pass is stratified and squamous, for blood draining the rumen, reticulum and to a lesser extent the omasum carries a high concentration of volatile acids while blood draining the abomasum and small intestine contains only traces. Of the acids present, acetic predominates and forms from 60 to 70% of the mixture, the remainder being composed of propionic and butyric acids. Propionic acid is the only one of the

it must be admitted that our efforts to utilize hormonal treatments for improving lactational performance in women, based upon our results with animals, have so far met with little success.

Similarly the relation between the hormones and the sex urge in woman is far more complex than in the lower mammals in which the urge to mate in the female simply results from treatment with ovarian hormones.

Again, studies on lower mammals and even insects, though very fruitful in adding to our knowledge of the genesis of hermaphrodism may be of little help to the clinician confronted by the problem of deciding how to treat a case of human hermaphrodism with its especial social and psychological considerations.

Dr. John Hammond: Having had considerable experience in the transference of the results obtained in one species to another, I am convinced that it is a very useful method with which to attack important problems. It is necessary, however, if bad mistakes are to be avoided, to understand thoroughly the physiology of the species concerned, before the results obtained in one species are applied to another. There is at present a need for more knowledge on the interrelationship between nutrition and endocrinology, for example, it has been suggested that the administration of vitamin E assists in cases where a deficiency of progesterone occurs in preventing abortion. There are, however, no exact experiments on this point. The whole subject of vitamins and trace elements in relation to internal secretion needs further exploration.

Dr. Arthur Walton: The comparative method may be the only possible approach to important problems which affect man. For example, in the analysis of male fertility the ultimate criterion of fertilizing capacity is the number of young, or of pregnancies, for a given number of matings. For obvious reasons the number of offspring from a man never exceeds a very small figure and individual births are distributed over a long period. The potential fertility of a man at any given time cannot therefore be assessed from his breeding record with any high degree of accuracy or statistical significance.

At one time it was common to assume that a male was fertile if a few active spermatozoa were found in the ejaculum.

Investigation of male fertility in rabbits revealed the fact that fertilization by any one spermatozoon was an event of very small probability, that the probability of fertilization was a function of sperm number and viability. and that the probability only reached a high level if the number of spermatozoa was large. It is now an established procedure to examine the semen of the male partner in childless marriages, whose responsibility may be as high as 50% of cases. The clinical tests applied are based upon results obtained with experimental animals.

Similarly, analysis of the endocrinology of spermatogenesis is based upon animal experimentation. It is important to determine to what extent the number and viability of the spermatozoa produced by the testis is dependent upon endo-secretions. The production of ova by the ovary is clearly dependent upon the level of gonadotrophic hormones in the blood, and over a wide range of dosage the number of ova produced is a function of the dose. If one ovary is removed surgically in experimental animals, the remaining ovary now produces double the normal number of ova, showing that the limit of ovum formation is not set by the anatomical limitations of the ovary but by the level of gonadotrophic hormones in the blood-stream.

In the case of the male, however, the relationship is not so clear. In the sexually mature animal little or no response is obtained from the injection of gonadotrophic hormones and recent experiments on rabbits have shown that after hemi-castration the output of the remaining testis remains the same.

Such experiments as described here cannot be done on the human, therefore there must be less certainty attached to hormone-therapy applied to this subject. The reaction of the human testis may be significantly different from that of the lower animals, but it would be unscientific to neglect the results obtained in animals in formulating human praxis.

Mr. Alastair N. Worden: The B vitamins furnish many examples of the limitations and uses of the comparative method. The search for the pellagra-preventive factor was greatly complicated by the study of "rat pellagra", which was a distinct deficiency. Canine blacktongue and pig pellagra were, however, analogous to human pellagra, and were

Section of Experimental Medicine and Therapeutics

President—R. D. LAWRENCE, M.D.

[*March* 14, 1944]

DISCUSSION, ON INFECTIVE HEPATITIS, HOMOLOGOUS SERUM HEPATITIS AND ARSENOTHERAPY JAUNDICE

Transmission Experiments in Animals and Man with Material from Infective Hepatitis and Homologous Serum Jaundice [*A Review*]

Dr. F. O. MacCallum: It is presumed that the hypothetical virus causing infective hepatitis is the same throughout the world though there may be different strains of it and the mode of transmission may differ in various climates.

The details of the work done in recent years are set out in tabular form. It will be seen that positive results have been reported in only two laboratories, in the pig experiments of Andersen and Tulinius in Denmark and the chick embryo and canary experiments of Siede and Dresel and their colleagues in Leipzig.

"As pigs were found to be affected with a form of jaundice resembling epidemic infective hepatitis in man in Denmark, the possibility of humans being infected by pork was examined. Epidemiological studies show that the number of jaundiced pigs delivered from the abattoirs have sufficed to explain the epidemics of infective hepatitis in Denmark." This quotation from Andersen's original paper reveals the basis of his experiments. He reported that the disease in pigs could be transmitted experimentally to young pigs on a quantitatively deficient diet by feeding them livers of jaundiced pigs. An increase in the icterus index of the serum and necrosis of liver cells was said to have occurred two to four days after feeding the infected livers. None of the pigs died but were killed at intervals. The same results were reported following the feeding of duodenal juice from human cases of infective hepatitis to supposedly normal pigs. Other workers have failed to confirm the results of the Danish workers. Hepatitis is rarely if ever seen in pigs in England. We have recently tried to repeat these experiments at Cambridge with the help of Mr. Venn of the Field Laboratories, Institute of Animal Pathology. Liver from fatal cases of acute yellow atrophy (either presumed infective hepatitis or following arsenotherapy) was suspended in nasal washings and duodenal juice from patients with infective hepatitis in the pre-icteric stage or on the first day of jaundice. The suspension was fed to 14 young pigs maintained on a quantitatively reduced diet. The results were entirely negative.

The Leipzig workers have reported deaths in chick embryos following inoculation on to the chorioallantoic membrane of duodenal juice collected in the pre-icteric stage of infective hepatitis and infection of canaries inoculated with filtered urine or duodenal juice collected at the same stage of the disease. The urine which is said to infect canaries produces no change in the chick embryos whilst blood which from human experiments may be presumed to be infected does not affect either chick embryo or canary. Numerous other workers have failed to confirm these results in the chick embryo and we have failed to infect 20 English canaries.

It thus appears that a universally satisfactory experimental animal has not yet been encountered.

The results of experiments in human volunteers indicate that blood from patients with infective hepatitis in the pre-icteric stage and up to two days after the appearance of jaundice is infective for man. Duodenal juice also appears to contain the infective agent in the pre-icteric stage. Neither of these findings indicates the portal of exit of the virus, but they suggest that both urine and fæces might contain the infective agent.

The animal experiments with material from cases of so-called homologous serum jaundice have been entirely negative.

From the experiments of Findlay and Martin in human volunteers one would deduce that there was an icterogenic agent in the nasal secretions of their cases of homologous

three which is recognized to be a glycogen precursor, consequently, in animals at grass, the exogenous supply of carbohydrate is small unless a significant part of the carbohydrate is transported to the small intestine from the rumen in the form of bacterial polysaccharide. In any case the nutritional problem which arises is intriguing and some light is thrown on the apparent ease with which ketogenic conditions occur in ruminants for both acetic and butyric acids are ketogenic, especially when the liver is low in glycogen. In this respect the question arises whether or not the ketone bodies themselves are toxic, for organs such as the heart and mammary gland are capable of destroying considerable quantities of β-hydroxybutyric acid.

Mr. John B. Brooksby : The study of the endocrine function of the placenta is a good example of an undertaking which cannot be dealt with directly in all species. It will be interesting to see if the anatomical variation of the maternal and fœtal circulation barrier in different species is correlated with the endocrinological functions. Newton and others have demonstrated that, in rodents at least, the placenta is associated with the hormonal control of many of the changes of late pregnancy, notably the development of the mammary gland, the maintenance of an abnormal body-weight until term, and the parturient alterations in the pelvic girdle. It is difficult to see how such data could be obtained without the use of the experimental animal.

Dr. R. L. Worrall : Limitations of the comparative method are well illustrated by diarrhœa and vomiting of infants, a disease which cannot be traced to one specific organism by means of bacterial cultivation and animal inoculation. Organisms which are non-pathogenic in the adult human intestine, e.g. strains of *B. coli* or enterococci, may prove to be pathogenic to infants under certain gastro-intestinal conditions. The work of E. F. Gale at Cambridge indicates that in some infants a streptococcus causes diarrhœa and vomiting through the formation of toxic amines in the lower bowel, when bacterial fermentation of sugar produces there an abnormally high degree of acidity.

Such hyperacidity in the lower bowel appears to arise when conditions in the stomach and upper intestine permit an excessive growth of sugar-fermenting bacteria. Twenty years ago, W. M. Marriott showed that cow's milk, in taking up three times as much acid as human milk, creates hypo-acidity in the artificially fed infant's stomach, and so promotes there the growth of bacteria which would otherwise be inhibited by the acidity of the gastric juice. In this connexion, Azim el Gholmy has recently found that *B. coli* could frequently be isolated from the gastric and duodenal contents of Egyptian infants suffering from diarrhœa, but not of healthy infants.

I am at present investigating a chemotherapeutic compound which is bacteriostatic to a wide range of the intestinal flora. But if the administration of this compound cures diarrhœa and vomiting of infants, I shall not be able to point to one particular organism as the cause of the disease. The problem awaits a final solution from those who can adapt the comparative method to this serious disease of infants.

Dr. W. R. Wooldridge said that the comparative method enabled an investigator to piece together the series of results obtained from experiments upon distinct but related problems. From the results of individual experimental analyses, not always made even on the same species of animal, a comprehensive picture of the complex, dynamic equilibria of a living system could be built up and then tested as a whole.

Section of Experimental Medicine and Therapeutics

President—R. D. LAWRENCE, M.D.

[March 14, 1944]

DISCUSSION, ON INFECTIVE HEPATITIS, HOMOLOGOUS SERUM HEPATITIS AND ARSENOTHERAPY JAUNDICE

Transmission Experiments in Animals and Man with Material from Infective Hepatitis and Homologous Serum Jaundice [*A Review*]

Dr. F. O. MacCallum: It is presumed that the hypothetical virus causing infective hepatitis is the same throughout the world though there may be different strains of it and the mode of transmission may differ in various climates.

The details of the work done in recent years are set out in tabular form. It will be seen that positive results have been reported in only two laboratories, in the pig experiments of Andersen and Tulinius in Denmark and the chick embryo and canary experiments of Siede and Dresel and their colleagues in Leipzig.

"As pigs were found to be affected with a form of jaundice resembling epidemic infective hepatitis in man in Denmark, the possibility of humans being infected by pork was examined. Epidemiological studies show that the number of jaundiced pigs delivered from the abattoirs have sufficed to explain the epidemics of infective hepatitis in Denmark." This quotation from Andersen's original paper reveals the basis of his experiments. He reported that the disease in pigs could be transmitted experimentally to young pigs on a quantitatively deficient diet by feeding them livers of jaundiced pigs. An increase in the icterus index of the serum and necrosis of liver cells was said to have occurred two to four days after feeding the infected livers. None of the pigs died but were killed at intervals. The same results were reported following the feeding of duodenal juice from human cases of infective hepatitis to supposedly normal pigs. Other workers have failed to confirm the results of the Danish workers. Hepatitis is rarely if ever seen in pigs in England. We have recently tried to repeat these experiments at Cambridge with the help of Mr. Venn of the Field Laboratories, Institute of Animal Pathology. Liver from fatal cases of acute yellow atrophy (either presumed infective hepatitis or following arsenotherapy) was suspended in nasal washings and duodenal juice from patients with infective hepatitis in the pre-icteric stage or on the first day of jaundice. The suspension was fed to 14 young pigs maintained on a quantitatively reduced diet. The results were entirely negative.

The Leipzig workers have reported deaths in chick embryos following inoculation on to the chorioallantoic membrane of duodenal juice collected in the pre-icteric stage of infective hepatitis and infection of canaries inoculated with filtered urine or duodenal juice collected at the same stage of the disease. The urine which is said to infect canaries produces no change in the chick embryos whilst blood which from human experiments may be presumed to be infected does not affect either chick embryo or canary. Numerous other workers have failed to confirm these results in the chick embryo and we have failed to infect 20 English canaries.

It thus appears that a universally satisfactory experimental animal has not yet been encountered.

The results of experiments in human volunteers indicate that blood from patients with infective hepatitis in the pre-icteric stage and up to two days after the appearance of jaundice is infective for man. Duodenal juice also appears to contain the infective agent in the pre-icteric stage. Neither of these findings indicates the portal of exit of the virus, but they suggest that both urine and faeces might contain the infective agent.

The animal experiments with material from cases of so-called homologous serum jaundice have been entirely negative.

From the experiments of Findlay and Martin in human volunteers one would deduce that there was an icterogenic agent in the nasal secretions of their cases of homologous

serum jaundice. The agent is present in the serum in the pre-icteric stage and has been isolated from the serum of a presumed case as long as seven days after the appearance of jaundice but was absent sixty-six days after the onset of jaundice. The agent which has been found in pools of supposedly normal human serum is capable of surviving a temperature of 56° C. for an hour but is inactivated by radiation with ultraviolet light. There is suggestive evidence that the agent may be cultivated in tissue cultures of minced chick embryo.

There are many debatable points in favour of and against the identity of infective hepatitis and homologous serum jaundice but there is no conclusive evidence one way or the other. It is essential to find a satisfactory susceptible experimental animal before much further knowledge can be obtained.

BIBLIOGRAPHY

ANDERSEN, T. T. (1937) *Acta. med. scand.*, 93, 209.
——, and TULINIUS, S. (1938) *Acta med. scand.*, 95, 497.
CAMERON, J. D. S. (1943) *Quart. J. Med.*, 12, 139.
DRESEL, E. G., MEDING, B., and WEINECK, E. (1943) *Z. ImmunForsch.*, 103, 129.
FINDLAY, G. M., DUNLOP, J. L., and BROWN, H. C. (1931) *Trans. R. Soc. trop. Med. Hyg.*, 25, 7.
——, MacCALLUM, F. O., and MURGATROYD, F. (1939) *Trans. R. Soc. trop. Med. Hyg.*, 32, 57.
——, and MARTIN, N. H. (1943) *Lancet* (i), 678.
FOX, J. P., MANSO, C., PENNA, H. A., and PARA, M. (1942) *Amer. J. Hyg.*, 36, 68.
HOYLE, L. (1943) *Med. Res. Coun., Monthly Bull. Min. Hlth. and Emerg. Publ. Hlth. Lab. Service*, 2, 99.
LAINER, G. (1940) *Wien. klin. Wschr.*, 53, 601.
MacCALLUM, F. O., and BAUER, J. (1944). In the Press.
OLIPHANT, J. W., GILLIAM, A. G., and LARSON, C. L. (1943) *Publ. Hlth. Rep. Wash.*, 53, 1233.
SIEDE, W., and LUZ, K. (1943) *Klin. Wschr.*, 22, 70.
——, and MEDING, G. (1941) *Klin. Wschr.*, 20, 1065.
VAN ROOYEN, C. E., and GORDON, I. (1942) *J. R. Army med. Cps.*, 79, 21..
VOEGT, H. (1942) *Münch. med. Wschr.*, 89, 76.

INFECTIVE HEPATITIS

ANIMAL TRANSMISSION EXPERIMENTS

Author	Material	Source	Animals inoculated	Route	Result
ANDERSEN and TULINIUS (1937-38, Denmark)	Duodenal washings	Man, in initial stage of disease	Pigs on reduced diet	*Per os*	Typical liver lesions
	Blood	Man, in initial stage of disease	Pigs on reduced diet	I.V.	1 pos., 1 neg.
	Livers	Pigs with porcine hepatitis	Pigs on reduced diet	*Per os*	Typical liver lesions
	Livers	Pigs fed duodenal washings	Rats	Injected	1 positive not repeatable
	Rats	Fed on porcine hepatitis livers	Pigs	*Per os*	Typical liver lesions
	Rat	Found in sty of a jaundiced pig	1 pig	*Per os*	Typical liver lesions
	Liver	Pig fed human duodenal juice	Rats	*Per os*	Fatal to rats and 3 passages but not repeatable
	Not stated	Not stated	Guinea-pigs, hens chor.all. memb.	*Per os*	Negative Negative

"Lesions in pigs fed with human material were somewhat less severe as the infection caused by feeding duodenal juice is presumably less massive."

Author	Material	Source	Animals inoculated	Route	Result
CAMERON (1943, Palestine)	Whole blood, plasma, leucocytic sediment	Pre-icteric pyrexial, icteric pyrexial, icteric non-pyrexia	Monkeys, guinea-pigs, dogs, mice, rats, hamsters, chick embryos	I.C., S.C., I.N., I. Cardiac, I.Hep., I.P.	Negative
	Nasopharyngeal washings	Cases of inf. hep.	Mice, guinea-pigs	I.N., I.P., I.C.	Negative
	Whole blood and serum	Cases of inf. hep.	6 horses	I.M.	Negative
DRESEL, MEDING, WEINECK (1943, Leipzig)	7 urines	Pre-icteric or first-day jaundice	Canaries	I.M.	2 to 3 passages
	1 urine	Pre-icteric or first-day jaundice	Canaries	I.M.	9 passages
	9 urines	Seventh-day jaundice or relapse	Canaries	I.M.	Negative
	Duodenal fluid and urine	3 patients	Canaries	I.M.	(1) Both positive. (2 and 3) Duodenal content only was positive
	Blood Duodenal juice and infected canary livers	Infective hepatitis	Canaries Chor all. memb.	I.M.	Negative Death of embryo 4 to 5 days
FINDLAY, DUNLOP and BROWN (1931, England)	Blood	4 pre-icteric; 1 first-day jaundice	10 *M. mulatta*	I.P.	Negative
	Nasopharyngeal washings	1 case pre-icteric	2 *M. mulatta*	"Sprayed"	Negative
	Blood	Pre-icteric stage	Mice, rats	I.P., I.C.	Negative
	Blood	Pre-icteric and icteric stages	Rabbits	I.V.	Negative
	Nasopharyngeal washings	Icteric stage	Rabbits	I. Tracheal	Negative
	Blood	Icteric stage	Guinea-pigs	Scarification, I.P.	Negative

ANIMAL TRANSMISSION EXPERIMENTS (*contd.*)

Author	Material	Source	Animals inoculated	Route	Result
FINDLAY, MacCALLUM, MURGATROYD (1939, England)	Whole blood serum, nasal washings, fæces, urine	Pre-icteric and first-day jaundice	M. mulatta, C. æthiops, hedgehogs, dogs, cats, ferrets, rabbits, guinea-pigs, field voles, rats, mice, fowl, pigeons. Chor.all. memb.	I.C., I.N., S.C., *Per os*, I.P.	Negative
	Duodenal contents and blood	Pre-icteric and first-day jaundice	6 pigs	*Per os* and injection	Negative
HOYLE (1943, England)	Blood, nasopharyngeal washings	Pre-icteric and first-day jaundice	Guinea-pigs and mice	I.N., I.P., I.C.	Negative
	Liver and spleen	Fatal case	Chor.all. memb.		Negative
LAINER (1941, Vienna)	"Extensive animal experiments were negative."				
SIEDE and LUZ (1943, Leipzig)	Duodenal juice	Early in disease	Chor.all. memb.		Death of embryo in 4 to 5 days. 1 to 8 passages.
SIEDE and MEDING (1941, Leipzig)	Duodenal juice	First-day jaundice	Chor.all. memb.		Death of embryo in 4 to 5 days. 3 passages
VAN ROOYEN and GORDON (1942, Middle East)	Bile and stomach washings	Icteric stage	Mice, white rats, jerboas, rabbits, guinea-pigs, C. æthiops, Abyssinian baboons, 1 young pig, 3 kittens	*Per os*	Negative
	Whole blood	Febrile pre-icteric and early icteric	Mice white rats, jerboas, rabbits, guinea-pigs, C. æthiops, Abyssinian baboons, 1 young pig, 3 kittens	I.C., Int. Corneal, I.V., I.P., S.C., Int. Test	Negative

HUMAN TRANSMISSIONS

Author	Material	Source	No. inoculated	Route	Result
CAMERON (1943, Palestine)	(1) 1·0 c.c. serum	Second-day jaundice	1	I.M.	Jaundice 35th day
	(2) Blood and nasal washings	From (1) stage not stated	1	Not stated	Neg. at 42nd day
	(3) 1 c.c. serum or 2·0 c.c. whole blood	Pyrexial stage	5	Not stated	(a) 1 jaundice, one month. (b) 1 ? positive at one month, jaundice at six months. (c) 3 jaundice at 2 to 6 months
	(4) Bed bugs	Fed on cases of infective hepatitis	Number not stated	Bite	Negative
LAINER (1940, Vienna)	300 c.c. blood from each of —	15 patients with infective hepatitis three to ten days after appearance of jaundice	Number not stated	Transfusion	Negative
	300 c.c. duodenal juice from —	15 patients as above	Number not stated	Introduced into duodenum by catheter	Negative
VAN ROOYEN and GORDON not experimental (1942, Middle East)	1 pint blood	Few hours before onset of symptoms	1	Transfusion	Negative
VOEGT (1942, Germany)	Duodenal juice	Pre-icteric stage	4	5·0 c.c. *per os*	2 jaundice, 2 positive
	Blood serum	Pre-icteric stage	1	5·0 c.c. S.C.	Positive
	Blood serum	Pre-icteric stage	1	5·0 c.c. I.M.	Positive
	Plasma	Pre-icteric stage	2	I.M.	?
	Urine	Pre-icteric stage	1	*Per os*	?
	Hæmolysed erythrocytes	Pre-icteric stage	1	*Per os*	1 positive

Positive = Rise in serum bilirubin with symptoms or evidence of liver damage measured by liver function tests.

HOMOLOGOUS SERUM JAUNDICE

ANIMAL EXPERIMENTS

Author	Material	Source	Animals inoculated	Route	Results
FINDLAY and MARTIN (1943, West Africa)	Not stated	Yellow-fever vaccine jaundice patients	Mice, guinea-pigs, rats, rabbits, 2 horses, baboons, cercopithecus, cercocebus and colobus monkeys	Not stated	Negative

ANIMAL EXPERIMENTS (*contd.*)

Author	Material	Source	Animals inoculated	Route	Results
FOX *et al.* (1942, Brazil)	Icterogenic yellow-fever vaccine		Baby chicks, guinea-pigs, *M. mulatta*	Not stated	Negative
	Blood serum and urine	Early stage of illness in yellow-fever vaccine jaundice	Rabbits, mice, guinea-pigs, *M. mulatta*	Not stated	Negative
	Liver	Fatal case	Chor.all. memb.	Not stated	Negative
MacCALLUM and BAUER (1944, England)	Blood	Yellow-fever vaccine jaundice, twenty-four to forty-eight hours' jaundice	Mice, rats, guinea-pigs, rabbits, *M. mulatta*, Syrian hamster	I.C., I.M., I. Cardiac, *per os*, S.C., I.P.	Negative
	Liver and spleen	Fatal case yellow-fever vaccine jaundice	Mice, rats, guinea-pigs, rabbits, *M. mulatta*, Syrian hamster	I.C., I.M., I. Cardiac, *per os*, S.C., I.P.	Negative
	Serum	Mumps convalescent plasma jaundice, pre-icteric stage	Mice, rats, guinea-pigs, rabbits, *M. mulatta*, Syrian hamster	I.C., I.M., I. Cardiac, *per os*, S.C., I.P.	Negative
	Bile-stained duodenal juice	Mumps convalescent plasma jaundice pre-icteric stage	*M. mulatta*	*Per os*	Negative
	Serum	Mumps convalescent plasma jaundice	2 horses	I.V.	Negative
	Serum	Homologous serum jaundice	Canaries, Chor.all. memb.	I.M.	Negative
OLIPHANT, GILLIAM and LARSON (1943, U.S.A.)	Icterogenic yellow fever vaccine		Monkeys, pigs, rabbits, guinea-pigs, white rats, Swiss mice, cotton rats, hamsters	Not stated	Negative
	Serum	Cases of yellow-fever vaccine jaundice	Monkeys, pigs, rabbits, guinea-pigs, white rats, Swiss mice, cotton rats, hamsters	Not stated	Negative

HUMAN TRANSMISSIONS

Author	Material	Source	No. inoculated	Route	Results
FINDLAY and MARTIN (1943, West Africa)	Nasopharyngeal washings	Twenty-four to forty-eight hours after onset of jaundice following yellow-fever vaccine	3	I.N.	1 jaundice 28 days 1 jaundice 30 days 1 jaundice 50 days
MacCALLUM and BAUER (1944, England)	(1) Serum	Seventh-day jaundice in a case of homologous serum jaundice	5	S.C. (0·5 c.c.)	2 jaundiced
		Seventh-day jaundice in a case of homologous serum jaundice	5	I.N. (1·0 c.c.)	1 jaundice 1 positive
	(1) Serum	Sixty-six days after onset of jaundice above	5	S.C	Negative
	(1) Serum	One hundred and forty-one days after onset of jaundice above	5	S.C.	Negative
	Tissue cultures of this serum	9th subculture (dilution 10⁷) of original serum	5	S.C	2 positive
	(2) Serum	Pooled human serum from blood bank (65 litres)	11	S.C. (0·5 to 2·0 c.c.)	4 jaundice 2 positive
	(2) Serum	Pooled human serum from blood bank (65 litres)	5	I.N. (2·0 c.c.)	1 ? positive (not jaundiced)
	Tissue culture of (2)	10th subculture	5	S.C.	Negative
	Chick embryo passage of serum (2)	4th to 7th passage	5	I.N., S.C	Negative

Positive = Sustained rise in level of serum bilirubin with symptoms but no clinical jaundice after same incubation period as cases that became jaundiced.

?Positive = Sustained rise in level of serum bilirubin without symptoms, after same incubation period as cases that became jaundiced.

HOMOLOGOUS SERUM JAUNDICE

HUMAN TRANSMISSION

Author	Material	No. inoculated	Route	Jaundice
OLIPHANT, GILLIAM, LARSON (1943, U.S.A.)	(1) Icterogenic yellow-fever vaccine	50	S.C.	12
	(2) Above vaccine heated at 56° C. for 30 minutes	10	S.C.	2
	(3) Above vaccine radiated 2½ hours with U.V.L.— 1 hour at 2,650 Å units and 1½ hours at 2,537 Å units	10	S.C.	0
	(4) Pooled serum of 9 cases of jaundice in (1) dil. 1/5	10	S.C.	2
	(5) Pooled serum of 9 cases of jaundice in (1) dil. 1/3	20	S.C.	6
	(6) Pooled weekly specimens of a mild case in (1) 1/3	10	S.C.	0
	(7) Pooled weekly specimens of a mild case in (4)	10	S.C.	0
	(8) Pooled weekly specimens of a severe case in (1) 1/3	20	S.C.	3
	(9) Pooled weekly specimens in a moderately severe case in (1) 1/3	20	S.C.	1
	(10) Pooled weekly specimens in the pre-icteric stage in 1 case in (1)	14	S.C.	4
	(11) Single specimen of same patient as in (10) taken two and a half months after jaundice had subsided	15	S.C.	0

I.C. = Intracerebral; I.N. = Intranasal; I.P. = Intraperitoneal; S.C. = Subcutaneous; I. Hep. = Intra-hepatic; I.V. = Intravenous; I.M. = Intramuscular; I. test. = Intratesticular.

Homologous Serum Hepatitis

Dr. A. M. McFarlan described some of the findings in a study which the American Red Cross-Harvard Unit had made of an outbreak of hepatitis following mumps convalescent plasma. This outbreak and others had shown that occasional batches of serum or plasma gave rise to hepatitis about three months after inoculation in up to 50% of those inoculated. Although epidemiological findings and the study of groups of cases revealed some differences between infective hepatitis and homologous serum hepatitis, it was not possible to make a differential diagnosis in the individual case. It was therefore important that reports of cases of supposed homologous serum hepatitis should record the results of a search for cases of infective hepatitis in contacts and of an attempt to trace the source of the serum or plasma used. It was even more important that these investigations should be made where the transfusion of whole blood appeared to be the cause of the hepatitis, since the case against the whole blood was so far not proven.

An account of the outbreak will shortly be published. (Beeson, P. B., Chesney, G., and McFarlan, A. M.; McFarlan, A. M., and Chesney, G.; Hawley, W. L., McFarlan, A. M., and Steigman, A. J., with McMichael, J., and Dible, J.—three papers in the press.)

Post-Arsphenamine Jaundice

Major James Marshall, R.A.M.C. (*Command Venereologist, Eastern Command and London District*): Hepatitis and jaundice occur at all stages of acquired and congenital syphilis. As a complication of treatment, jaundice was described even before the days of arsenic. Jaundice can appear at any time during the arsenical treatment of syphilis, but there are certain times at which it tends to occur most frequently. First, there is a hepatitis seen about the sixth to fifteenth day after the first arsenical injection, and often only a part of a general toxico-dermal (Milian's) reaction. Secondly, there is the delayed hepatitis, with greatest incidence about one hundred days after the start of treatment.

Both types of hepatitis can occur during or after the rapid treatment (five to thirty days) and in the long treatment of syphilis. It is possible for a patient to have an early and a delayed hepatitis with either type of treatment.

Early hepatitis.—The early hepatitis which occurs about the ninth day of treatment is commoner in intensive than in long treatment. It varies in severity from an increase in urobilinogen excretion found on routine examination to a frank icterus, but is usually mild and transient. Lloyd Jones and Maitland of the British Navy had three such early cases of jaundice in 100 intensive treatments with Mapharside of fifteen to thirty days' duration. Myers stated that the American Army in Britain had six early hepatitis cases in 750 twenty-day intensive treatments for early syphilis. All U.S. cases were accompanied by evidence of a toxico-dermal reaction of sensitization. The percentage incidence is markedly lower in the American series although the dosage of arsenoxide was generally higher than in the British Navy series of Lloyd Jones and Maitland. An important difference was that the Americans had a high carbohydrate and protein (120 g./day) diet whereas the British were on standard rations. The assumption is, however, that this type of hepatitis is a true toxic arsenical reaction.

Delayed hepatitis.—The delayed jaundice or hepatitis of the twelfth to seventeenth week after arsenical treatment starts is the commonest variety and is what is generally known as post-arsphenamine jaundice. This can occur in the treatment of any type or stage of syphilis in the adult.

Clinically post-arsphenamine jaundice is indistinguishable from infective hepatitis, biochemically no significant difference between the two has been shown so far, and pathologically Dible and McMichael have demonstrated by liver biopsy that the changes in the liver are the same in both diseases. Post-arsphenamine jaundice varies in severity from the mildest form with the faintest icterus and minimal symptoms to a fatal acute yellow atrophy. Abortive or subclinical hepatitis is quite common.

ÆTIOLOGY

Hepato-recurrence.—Milian's theory that jaundice coincident with treatment may be a hepato-recurrence of syphilis is not really tenable. If it were true one would expect sometimes to find other evidence of relapse apart from the liver. Such evidence is not seen, however, and unless all anti-syphilis treatment is suspended for a long period during or after hepatitis there is no evidence that the complication affects the ultimate prognosis of syphilis one way or the other. Although bismuth treatment of syphilis ought to continue through hepatitis there is good evidence, clinical and biochemical, that arsenic should be suspended until the liver has completely recovered.

Hepatitis occurring as part of a mucocutaneous relapse of syphilis is a different story and is not a contra-indication to the use of arsenicals.

Arsenic.—It is certain that arsenic itself has some part in the ætiology of the late post-arsphenamine jaundice, but it is not the prime factor and may not even be the most important. Increasing the total dose of arsenic over a given time has been shown by Curtis to increase the incidence of jaundice. He quotes from the records of the Whitechapel Clinic where an increase in dosage from 7·5 g. to 13 g. of an arsphenamine in a thirteen-week course caused an increase in jaundice incidence from 7 or 8% to 25 to 30%.

Marked reduction of the dose of arsenic by the use of arsenoxide instead of neoarsphenamine, the drug commonly used in Britain, has been said to reduce the incidence of jaundice. It is my own impression, and this is confirmed by some of my colleagues, that in the long treatment of syphilis when arsenoxide is used in what I consider adequate dosage, that is by twice weekly injections of the full dose, there is no significant change in incidence of jaundice. In the British Army, a reduction in dosage in the standard ten-week course of arsenical treatment from a total of about 6 g. of neoarsphenamine to about 4 g. had no obvious effect in reducing the incidence of jaundice. (A minimum of four such courses is given in early syphilis.) No particular brand or batch of neoarsphenamine has ever been incriminated in any of my clinics as especially liable to produce jaundice.

Variations in incidence.—Post-arsphenamine jaundice has long been observed to parallel in rate of incidence the infective hepatitis rate in the non-syphilitic population. This was noted by Ruge in Germany and by many others. The syphilitic is, however, much more liable, possibly twenty to forty times more liable, to jaundice than the otherwise healthy person. This is true at the present time as has been shown by Mitchell in the Canadian Army in Britain. The incidence of post-arsphenamine jaundice is inclined to rise in times of economic stress, with consequent dietary deficiency, as was pointed out by V. E. Lloyd and others.

At this time we may recall that in places such as West Africa where the staple diet is very low in protein the incidence of all types of liver disease is very high. The present increase in incidence of jaundice began in my area, Eastern England, in early 1941, reached its highest level about mid 1942, and has remained high ever since. The rate of rise was not the same in all areas. It was first observed south and southwest of London and a little later in London itself. Marked rise in incidence was only obvious in the eastern counties late in 1942 and in 1943. The incidence varies enormously in different clinics and in different parts of the country and has varied in my area from about 20 to about 50% in different places at the same time.

An odd circumstance is that the incidence of jaundice in civil V.D. clinics and in R.A.F. personnel in the same area is very much lower than in the military clinics although the routine of treatment, drugs, and methods of sterilization of equipment are not materially different. The incidence of jaundice in officers is at least as high as in soldiers. In peacetime the counterpart of the officer, the private patient, practically never got jaundice.

Women seldom get post-arsphenamine jaundice. The incidence in my own female clinics, civil and military, is well under 5%. The Service women under my direct care are treated exactly the same way as the men and with the same syringes.

Sulphydryl amino-acids. There is no doubt that diet is an important factor in the problem of post-arsphenamine jaundice. Whipple and others have demonstrated the protective powers of sulphur-containing amino-acids against liver damage after the administration of chloroform and other liver poisons. Working under the direction of Professor John Beattie, I have carried out a number of experiments to assess the value of the sulphur-containing amino-acids as prophylactic agents against post-arsphenamine jaundice. The majority of syphilitics who get jaundice get it at or about the hundredth day or about the time of the eleventh injection of arsenic under the army routine scheme. Prophylactic treatment was started before the peak of incidence and was carried beyond it. Control cases were also observed, and in this group the incidence of jaundice at about the hundredth day was about 50%. The materials used in the experiments were: (1) Papain digest of pure casein; (2) digest with added cystine; (3) pure cystine; (4) pure methionine.

The papain digest alone was of no value. Digest plus cystine and pure cystine were effective, and methionine is also effective although this experiment is not yet complete.

The results can be summarized by saying that so far as I have gone, the incidence of hepatitis has not been reduced, but that the time of appearance of jaundice can be altered, and this is important from the point of view of the syphilis treatment as I shall explain later. In the successful experiments with digest plus cystine and pure cystine about 50% of patients showed minimal signs of hepatitis around the hundredth day, but these signs were transitory and arsenical treatment continued to the twentieth injection, i.e. to the end of the second treatment phase. After cessation of prophylaxis and when the third treatment phase began, these same patients developed post-arsphenamine jaundice. The jaundice was treated with the protective amino-acids and it was of interest to note that those who were protected with cystine alone did not respond to cystine treatment for the jaundice, but did respond to treatment with digest plus cystine.

The explanation suggested is that the important amino-acid is methionine, which was a constituent of the digest, and that cystine may have a limited action in sparing methionine.

The work with pure methionine is not yet far enough advanced to give any final results, but it can be said that the incidence of hepatitis at the hundredth day has been reduced.

The value of these seemingly inconclusive results is this: The partial protection afforded these men enabled them to have their first twenty arsenical injections regularly and without interruption by jaundice. This would certainly enhance their chance of a rapid cure of their syphilis which is jeopardized if arsenical treatment is interrupted at about the eleventh injection as is the case when jaundice appears at the usual time.

Syringe infection.—Until recently syringes in my clinics and most others have been sterilized by washing in running water followed by immersion in methylated spirits. The possibility of transmission of an infective agent by syringes used for intravenous injection of arsenic has been suggested. There are many pointers that this is the case. In order to try to prove the point some patients with syphilis at one of my hospitals were each given a special new syringe and needle, boiled before and after injections, and used by no other patient. Many patients were started but postings reduced the number who continued for sufficient time to be relevant to only six cases. Not one developed jaundice at or about one hundred days after treatment started. The incidence in controls was 50%.

One of the six is interesting: He had his first injection on 26.5.43. His eleventh and twelfth injections were given at a civil clinic while he was on leave on 2 and 8.9.43. They were given with a syringe used for other patients and sterilized in methylated spirits. Subsequent injections were given with his own syringe. Eighty-three days after his first injection at the civil clinic he showed signs of liver damage and subsequently became jaundiced.

Again, in my records I have found cases coming into my clinic after treatment in other areas where jaundice incidence is low, and developing jaundice while under my care. In eight such cases jaundice developed between 190 and 405 days after the first arsenical injection. The lapse between the first injection at my clinic, where incidence is high, and the first sign of jaundice lay between 89 and 110 days. This is certainly suggestive of an infection occurring on changing clinics. The same phenomenon has been noted at another of my hospitals.

I have also seen and heard of non-syphilitic patients who, given intravenous injections of drugs of various kinds with syringes from venereal diseases departments, have developed jaundice about a hundred days later.

Differences between infective hepatitis and post-arsphenamine jaundice.—It would appear that the only outstanding difference between post-arsphenamine jaundice and infective hepatitis is in length of incubation period and in mode of spread.

The incubation or latent period for post-arsphenamine jaundice is about one hundred days and spread is probably by infected syringes. In infective hepatitis the incubation period is about thirty days, spread is probably by droplet infection, and according to Pickles an immunity is conferred comparable with that after measles.

Professor Beattie and I have noted in one hospital where post-arsphenamine jaundice and infective hepatitis cases are treated in the same ward a number of instances where post-arsphenamine jaundice cases have had another attack of jaundice about thirty days after they left hospital. This, and other evidence, suggested that they had been infected with infective hepatitis, or thirty-day jaundice, while in hospital. None of the cases of infective hepatitis relapsed after leaving hospital. If our assumption is correct it would mean that an attack of post-arsphenamine jaundice confers no immunity against infective hepatitis.

SUMMARY

Post-arsphenamine jaundice has an incubation period of about one hundred days and is probably due to a combination of factors: (1) An infective factor introduced by syringe; (2) dietetic deficiency of protein with emphasis on sulphur-containing amino-acids; (3) arsenic.

Its control lies in: (1) Proper sterilization of syringes in venereal diseases clinics; (2) increase in diet, particularly in protein.

As far as treatment of established jaundice is concerned, I wish to say emphatically that the high carbohydrate and low fat and protein diet advocated in the past and used still by the majority of doctors is quite useless. The best results are obtained with a high protein, high calorie diet, chosen at the discretion of the patient, supplemented by two pints of dried or fresh milk and an egg, dried or fresh, each day.

REFERENCES

ANWYL-DAVIES, T. (1943) *J. R. nav. med. Serv.*, 29, 153.
BEATTIE, J., and MARSHALL, J. (1944) *Brit. med. J.* (i), 547.
BIGGER, J. W. (1943) *Lancet* (i), 457.
CURTIS, F. R. (1942) *Lancet* (ii), 351.
DIBLE, J. H., McMICHAEL, J., and SHERLOCK, S. P. V. (1943) *Lancet* (ii), 402.
LLOYD-JONES, T. R., and MAITLAND F. GORDON, (1943), *Brit. med. J.* (i), 448.
LLOYD, V. E. (1943) *Brit. J. Vener. Dis.*, 19, 64.
MARSHALL, J. (1943) *Brit. J. vener. Dis.*, 19, 52.
MILIAN, G. (1920) *Bull. Soc. méd. Hôp. Paris*, 44, 226.
MILLER, L. L., ROSS, J. F., and WHIPPLE, G. H. (1940) *Amer. J. med. Sci.*, 200, 739.
——, and WHIPPLE, G. H. (1940) *Amer. J. med. Sci.*, 199, 204.
—— —— (1942) *J. exp. Med.*, 76, 421.
MITCHELL, H. S. (1943) *Canad. med. Ass. J*, 48, 94.
MYERS, J. (1944) January Meeting of Med. Soc. for Study of V.D.
RUGE, H. (1927) *Arch. Derm. Syph.*, Berlin, 153, 518.
——, (1932) *Derm. Wschr.*, 94, 278.

Hepatitis Following Yellow-Fever Vaccinations

Lt.-Colonel Theodore L. Badger, U.S.A.M.C.: The epidemic of hepatitis in the United States Army that followed the preventive inoculations with yellow-fever vaccine appeared simultaneously in whatever part of the world United States Troops were stationed in the spring and early summer of 1942. Northern Ireland was the centre of nearly all cases appearing in the United Kingdom, but what occurred there was merely a sample of the outbreaks of jaundice in other theatres. The —— General Hospital cared for 1,318 cases of the disease on its wards from May 21, 1942, up to December 21, although the height of the epidemic had passed by mid-August.

The clinical picture of this acute hepatitis was marked by a subacute course, where symptomatic mildness was no consistent index of the severity of liver damage. The onset was one of gastro-intestinal complaints, of nausea and vomiting, variable abdominal pain, exhausting fatigue, great loss of weight, joint pains, and finally by the sudden appearance of dark brown urine and jaundiced eyes. A marked bradycardia, low blood-pressure, striking absence of fever throughout the entire course of the disease and a normal urine except for bile pigments were characteristic features. Slow disappearance of icterus, prolonged hepatomegaly, and an enduring fatigue marked the recovery period.

The ætiology of the jaundice was obscure but severe parenchymal disease of the liver was considered the essential pathological lesion. There appeared to be an association with the yellow-fever vaccinations from the start. In conjunction with Colonel John Gordon, then director of the American Red Cross Harvard Hospital, epidemiological studies of affected units were directed toward the incidence and the origin of the disease.

Two possibilities existed in regard to the yellow-fever vaccine as the source of the epidemic. The jaundice was either an attenuated form of yellow fever, resulting from

the living seed virus of the vaccine, or it arose from some factor contained in the normal human serum diluent. The preparation of the vaccine for immunization of troops was carried out by the inoculation of developing chick embryos with culture virus after many tissue culture passages. After incubation the virus inoculated embryo was minced and then suspended in normal human serum, filtered, adjusted to contain a standard amount of virus and then frozen and dried. From the make-up of the vaccine it appeared probable that if the seed virus were to blame a wide scattering of the jaundice among heterogeneous lot numbers was to be expected. If the serum diluent contained the jaundice-producing agent the disease would tend to occur in closely allied lots.

A few facts emerged from the surveys designed to reveal any relationship between the vaccine and the jaundice. A total of 80 lot numbers were encountered. 67 of these showed *no* associated jaundice. Only eight lots showed a significant attack rate of 3% or more. Five lots presented an insignificant attack rate of less than 1%. Those lots affected tended to appear in groups of closely allied numbers. One lot, No. 368, presented the same attack rate in two widely separated units. Thus emphasis was directed toward the human serum diluent as containing the jaundice-producing factor but the nature of this factor was in no way revealed. The possibility of altered virulence of the virus remained, however, and subsequent study was directed towards the clarification of the source of the agent in the vaccine. But if the living seed virus were the cause, in its attenuated or otherwise altered form, the clinical and laboratory evidence should verify it.

Clinical study of the jaundice, however, showed little evidence for the diagnosis of yellow fever and the absence of fever and renal involvement was inconsistent with any known form of the disease. Mouse-protection studies carried out for us by Dr. MacCallum at the Wellcome Laboratories showed no increase in protective antibodies against the yellow-fever virus over a period of weeks in all individuals studied. Thus it could be clearly stated that the jaundice was *not* yellow fever in any form, and therefore not due to the seed virus in the vaccine.

Evidence of communicability of the disease from person to person by contact was conspicuously absent. A control survey of the entire —— General Hospital personnel for evidence of jaundice was carried out in June 1942 at the start of the epidemic and again five months later at its completion. Over 1,300 cases of hepatitis were cared for by the staff and only a single case of jaundice developed. This one was unique in the accidental self-inoculation with serum from a patient seriously affected with jaundice at the start of his disease, which followed the use of a lot number of high attack rate. A second study of communicability was that of a coast artillery unit heavily affected with lot No. 368 having a high attack rate. Living within this unit in close proximity twenty-four hours a day was a group of 51 men who had never been inoculated with yellow-fever vaccine. None of these 51 men developed jaundice.

An examination of immunization records for the relationship of the appearance of jaundice to the date of immunization showed that twelve to eighteen weeks was the constant incubation or latent period between inoculation with yellow-fever vaccine and the development of jaundice. This was inconsistent with all other forms of infectious jaundice or yellow fever.

Virus studies, with animal inoculation of fresh duodenal washings and blood serum of pre-icteric and severe cases, were all entirely negative. But this evidence was inconclusive, and the resources were inadequate for exhaustive studies of virus disease.

One case only died of hepatitis, a mortality rate roughly of one in a thousand which is in accord with the rate in other epidemic theatres. The pathology of this one case presented no features distinguishing it from severe hepatitis with death from acute yellow atrophy, arsenical poisoning or the hepatitis following preventive vaccinations for measles and mumps.

In the Virgin Islands J. W. Oliphant studied the transmission of yellow-fever vaccine in human volunteers. Using specific lot numbers of yellow-fever vaccine he successfully reproduced the characteristic clinical picture of acute hepatitis by subcutaneous transmission of serum from person to person with the following specific observations: (1) The jaundice-producing agent was filtrable, it survived drying at +° C. for long periods, and it survived heating at 56° C. for thirty minutes in the dry state. (2) The agent appeared to be neutralized by one hour exposure to ultraviolet light. (3) The agent was present in the circulating blood before jaundice appeared. (4) The agent was not present two and a half months after disappearance of jaundice. Only one thing, however, could be definitely stated on the basis of clinical and laboratory proof, that the disease was not yellow fever in any form and therefore not due to reactivation of the seed virus. The hepatitis was apparently not spread by contact from person to person and it was no commonly known form of epidemic hepatitis. Evidence pointed toward the human serum diluent of the vaccine as containing the factor responsible for the jaundice but no

information was obtained as to whether the jaundice-producing factor was a virus, a chemical or physical agent or some allergenic product. We do know that since this epidemic all yellow-fever vaccine has been prepared without the human serum diluent and that as far as reports are available, no jaundice has followed its use.

Major M. H. Salaman, R.A.M.C.: I shall give an account of one aspect only of our work at the Royal Victoria Hospital, Netley, on jaundice occurring in men receiving intravenous injections of arsenic for syphilis, namely, the influence of the technique of injection on the incidence of the disease.

It has been suggested by Dr. F. O. MacCallum and others that post-arsenical jaundice may be spread from patient to patient by means of syringes imperfectly sterilized between injections. Lieut.-Colonel Bigger showed that the technique employed in many V.D. Clinics cannot be relied on to prevent the transference of an infective agent. Briefly this technique is as follows, with local variations.

At the beginning of the morning's work the syringes and needles are boiled. Before each injection some distilled water from a bottle labelled "Sterile" is poured into a gallipot, which has been boiled. The ampoule of the drug is opened, and the powder poured into the gallipot. The solution is taken up into a syringe, the needle inserted in the vein, some blood is withdrawn into the barrel, and the injection is given, leaving a small amount of solution in the syringe to prevent injection of air. The syringe and needle are rinsed through under the tap, the needle is removed for re-boiling, and the syringe is washed out in several changes of distilled water in kidney dishes, a number of syringes being rinsed before the water is changed. If there is an adequate supply of syringes they may be rinsed out, or allowed to lie for a short time, in weak lysol or biniodide, between the rinsings in water. Then a freshly boiled needle is fitted and the next injection given. The chief danger of this method arises from the sucking back of blood into the syringe. Col. Bigger showed that staphylococci mixed with blood, sucked into a syringe, were not completely removed or killed by a process of rinsing such as the above; they were not even reduced in number to the extent to be expected from simple dilution.

Substantially this technique has been in use for years in many V.D. Clinics. Before the war there was little to suggest that it was responsible for transference of infections. How then can it be blamed now for the enormous wartime rise in incidence of post-arsenical jaundice? First, the great increase in numbers of patients, and the shortage of syringes, have made the method much more dangerous than formerly. In a busy clinic there is not time for the syringes to lie in disinfectant for a sufficient time between injections. Second, the incidence of infective hepatitis in the general population has risen, and it is probable that the number of persons in an infective condition, that is to say, those in the prodromal stage of the disease, or healthy carriers, has increased also. Consequently the chance of transference is greater.

However this may be, we have taken the transference of infection by means of syringes as the working hypothesis in the following trial.

A technique of intravenous injection was devised which we believed would exclude the possibility of cross-infection. All glass syringes, lubricated with liquid paraffin, with needle attached, are sterilized by dry heat (150° to 160° C. for one hour) in separate test tubes. Screw-cap bottles containing approximately 10 c.c. distilled water are autoclaved. Before an injection, one orderly opens the ampoule of powdered mapharside, empties it into one of the water containers and replaces the screw cap, without touching the lips of ampoule or bottle with his fingers. The medical officer withdraws a sterile syringe from its tube and sucks up the whole of the solution, squirting in and out to complete solution, if necessary. Meanwhile another orderly has prepared the patient's arm. The drug is injected, and the syringe immediately handed to a third orderly, who rinses it out once under the tap and replaces it in its tube. The used syringes are returned to the laboratory for cleaning, lubricating, and re-sterilizing.

It was our original intention to treat alternate new cases of early syphilis with the above technique, and to treat the rest by the old technique; but this was soon found impracticable. In order to get a measure of the incidence in the two groups it was necessary to keep patients attending our clinic, without remission, for at least four months, owing to the long latent period of the disease. Everyone with experience of army venereal practice will realize the difficulty of doing this. It was soon apparent that we could only collect an adequate experimental group by including almost every new patient. In spite of strenuous efforts to keep these patients in the district only about one-third of them remained with us for four months. Patients of the experimental group mixed freely with others in the waiting room, which was often crowded, so that there was plenty of opportunity for possible droplet spread.

In order to provide adequate control for this experiment we have followed up a considerable number of patients, originally diagnosed at Netley and treated by the ordinary

technique, either wholly at Netley, or partly at Netley and partly at other clinics. Intravenous mapharside and an intramuscular bismuth preparation were used throughout. Comparison between the experimental and control groups was made after one hundred and twenty days, and again after one hundred and eighty days of treatment.

We should, of course, have liked to have had a control group strictly comparable in every way to the experimental, that is to say, treated completely at our clinic over the same period. This was not possible. The absence of such a group lays our results open to two possible criticisms. It can be said, firstly, that men treated wholly at our clinic may have a different jaundice incidence from those treated elsewhere, and secondly that there may be a seasonal change of incidence. I think we can answer these criticisms from the figures I have shown (Table I). Analysis of the control group shows that there is no significant difference in incidence among men treated with the ordinary technique between those whose treatment began between February and June 1943 and between July and November 1943, nor between those treated wholly at Netley and those treated partly at Netley and partly elsewhere. But the difference in incidence between these groups on the one hand, and the group treated by the new technique on the other, is, we believe, significant.

TABLE I—POST-ARSENICAL JAUNDICE

A.—INFLUENCE OF TECHNIQUE ON INCIDENCE

	Place of treatment and date of first injection	Followed for four months No. treated	Jaundice	Followed for six months No. treated	Jaundice
Old technique ...	...Netley and elsewhere Feb. to Nov. 1943	67	25	56	38
New technique ...	...Netley only July to Nov. 1943	29	1	12	1

B.—INFLUENCE OF TIME AND PLACE ON INCIDENCE

Old technique	...Netley only	23	7	18	12
	Netley and elsewhere	44	18	38	26
	Feb. to June 1943	53	18	44	28
	July to Nov. 1943	14	7	12	10

Instructions are now in force that all syringes must be boiled between every intravenous injection at all Army Clinics. I think the evidence which I have brought forward shows how necessary this change was. Nevertheless I myself do not believe that merely boiling syringes will meet the case. There are other possibilities of transference in a busy clinic, against which our technique was designed to guard. Syringes which have been boiled in tap water have to be rinsed in distilled water before use. The gallipot in which the drug is used stands on the bench for long periods and is used over and over again; the lip of the bottle of sterile water from which it is filled is likely to become contaminated. All these manipulations have to be carried out by attendants who are handling patients and blood-stained syringes. Clearly there is danger of transference of infection here, even if the syringes are boiled between injections. A closed method, such as the one I have described, obviates these dangers, and, once it is organized, is considerably easier and quicker in use than the old open method.

We must expect occasional cases, even if an ideal technique is followed. There will always be some of the epidemic type occurring. Moreover one cannot exclude the possibility that arsenic may activate an otherwise healthy carrier.

There is another type of post-arsenical jaundice which we have met, and which will, I think, also continue to occur whatever technique is used. It occurs early in treatment, usually between the fifth and twenty-fifth day; a sudden onset, with rigors, fever, vomiting, and sometimes a rash, is followed by jaundice. It is probably related to the syndrome known as "erythema of the ninth day" or Milian's syndrome. Arsenic given after recovery often causes another attack, unless given in very small and slowly progressive doses. An eosinophilia is common. The condition is probably due to a hypersensitivity to arsenic. We have records of five of these cases, of which one occurred in the experimental group recently. Others are recorded in the literature.

To summarize, we have shown that by means of a technique of injection designed to eliminate the possibility of transference of infection from patient to patient it is possible to reduce the incidence of post-arsenical jaundice very greatly. The incidence of post-arsenical jaundice in men treated by the ordinary technique for 120 days was about 40%, and for 180 days about 70%. The incidence in men treated by the new technique for 120 days was 1 out of 29, and for 180 days 1 out of 12.

I wish to thank Lieut.-Colonel A. J. King and Majors D. I. Williams and C. S. Nicol for their help in this investigation.

Dr. N. F. Maclagan : I want to refer very briefly to some results obtained with the serum colloidal gold reaction in jaundice which may have some bearing on the subject under discussion. While most liver function tests do not throw any light upon ætiology the newer flocculation tests appear to be in a separate class in this respect as they give strikingly different results in certain types of liver damage.

The serum colloidal gold reaction was performed by adding 2·5 ml. of gold sol to 0·05 ml. of serum under standard conditions of pH and ionic strength (Maclagan, 1944), a positive result being indicated by partial or complete precipitation of the gold. The reaction probably depends upon the presence in the serum of an excess of gamma globulin (Gray and Barron, 1943; Kabat *et al.* 1943), which is presumably liberated into the circulation by the damaged liver cells. The table shows the results in 189 cases of jaundice. 5 represents complete precipitation and is the strongest positive, while 0 represents no precipitation and is a negative or normal result. The test is mainly positive in infective hepatitis and negative in obstructive jaundice; it usually remains negative in obstructive jaundice even in the presence of gross liver damage as shown by other tests, thus demonstrating a qualitative difference in these two types of liver failure. The results particularly relevant to the present discussion are those in infective hepatitis—95% of 105 cases positive—and in arsenical jaundice (i.e. jaundice occurring during antisyphilitic treatment) in which only 42% of 50 cases were positive. This difference is statistically highly significant, being no less than 7·5 times its standard error ($53·2 \pm 7·1$). A similar preponderance of negative reactions in arsenical jaundice was noted by Hanger and Gutman (1940) with the cephalin-cholesterol flocculation test, but a parallel series of cases of infective hepatitis was not available for comparison.

The general similarity of the liver lesion in these two groups has been so much stressed recently that evidence of this type must be accepted with caution, but it does appear to indicate some essential difference in liver metabolism which demands an explanation. This is not likely to be found in the degree of liver damage which is probably at least as great in the arsenical group, as shown by the liver biopsy studies of Dible and McMichael (1943) and by other tests such as galactose tolerance and hippuric acid excretion. We are therefore left with two principal alternatives : Either arsenic modifies the response of the liver to infective hepatitis, or at least half of the arsenical cases are due to some agent different from that causing infective hepatitis. This agent could be either the arsenic itself, or an unusual strain of icterogenic virus. Unfortunately it is difficult at present to obtain any evidence which would decide between these two hypotheses, but they may possibly serve as a basis for future experiments.

I am much indebted to Major J. Marshall who has very kindly provided most of the arsenical sera used in this work.

SERUM COLLOIDAL GOLD REACTION IN 189 JAUNDICED PATIENTS

Precipitation number ...			5	4	3	2	1	0	Totals	% positive
Obstructive	...	...	–	–	–	2		32	34	6
Infective hepatitis ...	...	...	63	11	13	9	4	5	105	95·2
Arsenical ...	...	...	5	4	4	6	2	29	50	42

REFERENCES

DIBLE, J. H., and McMICHAEL, J. (1943) *Brit. J. Vener. Dis.*, **19**, 102.
GRAY, S. J., and BARRON, E. S. G. (1942) *J. clin. Invest.*, **22**, 191.
HANGER, F. M., and GUTMAN, A. B. (1940) *J. Amer. med. Ass.*, **115**, 263.
KABAT E. A., HANGER, F. M., MOORE, D. H., and LANDAU, H. (1942) *J. clin. Invest.*, **22**, 563.
MACLAGAN, N. F. (1944) *Brit. J. Exp. Path.*, **25**, 15.

Dr. John F. Loutit : Of the four clinical types of jaundice that have been described, two—the homologous serum jaundice and the yellow-fever vaccine jaundice—are almost certainly identical as human serum is common to both. Infective hepatitis, although it has similar clinical and histological features, may have a different causative agent. Post-arsphenamine jaundice appears to resemble the homologous serum jaundice, particularly as the syringes used for the administration of the arsphenamines are incriminated. These might well contain traces of blood aspirated from a previous recipient.

I have recently been able to study a series of cases of homologous serum jaundice, all following the administration of a particular batch of dried human serum. 17 cases received transfusions of up to 1,200 c.c. of the reconstituted material : 10 developed jaund⸱   received only 0·1 c.c. intradermally and 30 developed jaundice. The min⸱   just as effective as the very large dose in causing jaundice. It i⸱   ⁿ picture how traces of blood left in a syringe used for arsʲ   homologous serum jaundice.

Section of Odontology

President—HAROLD CHAPMAN, L.D.S.Eng.

[*January* 24, 1944]

The Pathology and Treatment of the Exposed Vital Pulp

By W. STEWART ROSS, L.D.S. R.C.S.Eng.

A CONSIDERABLE number of pulpless teeth treated by ordinary routine methods are subsequently found to develop peri-apical infection. In the case of anterior teeth such infection can be treated by the operation of root resection, but in the more inaccessible posterior teeth, this often involves the loss of the tooth.

It is the purpose of this paper to indicate how such teeth become infected, and what steps appear to be necessary to take to ensure that the apex does not become contaminated during treatment.

When the pulp is exposed as a result of caries it is always infected. The organisms, however, are usually confined in the first instance to a small corner of the pulp chamber opposite the exposure, whilst the rest of the pulp remains normal and uninfected.

When the crown of a normal healthy tooth is fractured, exposing the pulp, it may be uninfected, but if the pulp remains open to mouth fluids, organisms soon become implanted in the pulp chamber, when the condition resembles that of a carious exposure.

As a result of the invasion of organisms into the pulp tissue, the inevitable response of the tissues to infection occurs, and the phenomenon of inflammation is produced.

Polymorphonuclear leucocytes make their way from the neighbouring vessels to the site of the infection, to be followed later by lymphocytes, or round cells. As a result of the inflammatory exudate, the organisms are pinned down to a small area and their further extension checked.

But for the fact that the area of infection is surrounded by patent dentinal tubules into which the organisms can grow, there is little doubt but that the leucocytes would succeed in destroying the invaders, once the carious cavity was cleaned and filled. As it is, the organisms persist, and a chronic abscess is formed opposite the exposure, but usually the lesion does not remain in this condition for long. Much more often the inflammatory condition of the pulp leads to stasis and death of the pulp. As a result of the phagocytosis and inflammatory exudate, the pulp tissue becomes congested, and it would seem probable that, owing to the swelling at the apical portion of the root, the vessels carrying away the waste products become compressed. Often the more resilient afferent vessels continue to pump blood into the already engorged canal, with the result that stasis and death of the pulp occur. The dentinal tubules then become filled with blood which gives the tooth the familiar blue shade which changes to brown as the hæmosiderin crystals coalesce. The organisms are able to grow at will amongst the dead tissue and it is only a matter of time before they reach the peri-apical tissues.

The lapse of time from the initial exposure to the final death of the pulp varies considerably, and depends upon the position of the exposure and its size, which governs the amount of inflammatory exudate which can escape. If the cavity is situated on the biting surface, pieces of food débris are likely to be bitten into the carious cavity, and organisms are pushed further into the pulp, with the formation of an acute abscess. This interval may vary from a day to several months or even years, but at its commencement the patient is usually fully conscious of the fact that there is a pulp exposure,

Dr. N. F. Maclagan : I want to refer very briefly to some results obtained with the serum colloidal gold reaction in jaundice which may have some bearing on the subject under discussion. While most liver function tests do not throw any light upon ætiology the newer flocculation tests appear to be in a separate class in this respect as they give strikingly different results in certain types of liver damage.

The serum colloidal gold reaction was performed by adding 2·5 ml. of gold sol to 0·05 ml. of serum under standard conditions of pH and ionic strength (Maclagan, 1944), a positive result being indicated by partial or complete precipitation of the gold. The reaction probably depends upon the presence in the serum of an excess of gamma globulin (Gray and Barron, 1943; Kabat et al. 1943), which is presumably liberated into the circulation by the damaged liver cells. The table shows the results in 189 cases of jaundice. 5 represents complete precipitation and is the strongest positive, while 0 represents no precipitation and is a negative or normal result. The test is mainly positive in infective hepatitis and negative in obstructive jaundice; it usually remains negative in obstructive jaundice even in the presence of gross liver damage as shown by other tests, thus demonstrating a qualitative difference in these two types of liver failure. The results particularly relevant to the present discussion are those in infective hepatitis—95% of 105 cases positive—and in arsenical jaundice (i.e. jaundice occurring during antisyphilitic treatment) in which only 42% of 50 cases were positive. This difference is statistically highly significant, being no less than 7·5 times its standard error (53·2±7·1). A similar preponderance of negative reactions in arsenical jaundice was noted by Hanger and Gutman (1940) with the cephalin-cholesterol flocculation test, but a parallel series of cases of infective hepatitis was not available for comparison.

The general similarity of the liver lesion in these two groups has been so much stressed recently that evidence of this type must be accepted with caution, but it does appear to indicate some essential difference in liver metabolism which demands an explanation. This is not likely to be found in the degree of liver damage which is probably at least as great in the arsenical group, as shown by the liver biopsy studies of Dible and McMichael (1943) and by other tests such as galactose tolerance and hippuric acid excretion. We are therefore left with two principal alternatives: Either arsenic modifies the response of the liver to infective hepatitis, or at least half of the arsenical cases are due to some agent different from that causing infective hepatitis. This agent could be either the arsenic itself, or an unusual strain of icterogenic virus. Unfortunately it is difficult at present to obtain any evidence which would decide between these two hypotheses, but they may possibly serve as a basis for future experiments.

I am much indebted to Major J. Marshall who has very kindly provided most of the arsenical sera used in this work.

SERUM COLLOIDAL GOLD REACTION IN 189 JAUNDICED PATIENTS

Precipitation number ...	...	5	4	3	2	1	0	Totals	% positive
Obstructive	—	—	—	2	—	32	34	6
Infective hepatitis	63	11	13	9	4	5	105	95·2
Arsenical	5	4	4	6	2	29	50	42

REFERENCES
DIBLE, J. H., and McMICHAEL, J. (1943) *Brit. J. Vener. Dis.*, **19**, 102.
GRAY, S. J., and BARRON, E. S. G. (1942) *J. clin. Invest.*, **22**, 191.
HANGER, F. M., and GUTMAN, A. B. (1940) *J. Amer. med. Ass.*, **115**, 263.
KABAT E. A., HANGER, F. M., MOORE, D. H., and LANDAU, H. (1942) *J. clin. Invest.*, **22**, 563.
MACLAGAN, N. F. (1944) *Brit. J. Exp. Path.*, **25**, 15.

Dr. John F. Loutit : Of the four clinical types of jaundice that have been described, two—the homologous serum jaundice and the yellow-fever vaccine jaundice—are almost certainly identical as human serum is common to both. Infective hepatitis, although it has similar clinical and histological features, may have a different causative agent. Post-arsphenamine jaundice appears to resemble the homologous serum jaundice, particularly as the syringes used for the administration of the arsphenamines are incriminated. These might well contain traces of blood aspirated from a previous recipient.

I have recently been able to study a series of cases of homologous serum jaundice, all following the administration of a particular batch of dried human serum. 17 cases received transfusions of up to 1,200 c.c. of the reconstituted material: 10 developed jaundice. 54 cases received only 0·1 c.c. intradermally and 30 developed jaundice. The minute dose appeared to be just as effective as the very large dose in causing jaundice. It is not difficult, therefore, to picture how traces of blood left in a syringe used for arsphenamine can give rise to homologous serum jaundice.

Section of Odontology

President—HAROLD CHAPMAN, L.D.S.Eng.

[*January* 24, 1944]

The Pathology and Treatment of the Exposed Vital Pulp

By W. STEWART ROSS, L.D.S. R.C.S.Eng.

A CONSIDERABLE number of pulpless teeth treated by ordinary routine methods are subsequently found to develop peri-apical infection. In the case of anterior teeth such infection can be treated by the operation of root resection, but in the more inaccessible posterior teeth, this often involves the loss of the tooth.

It is the purpose of this paper to indicate how such teeth become infected, and what steps appear to be necessary to take to ensure that the apex does not become contaminated during treatment.

When the pulp is exposed as a result of caries it is always infected. The organisms, however, are usually confined in the first instance to a small corner of the pulp chamber opposite the exposure, whilst the rest of the pulp remains normal and uninfected.

When the crown of a normal healthy tooth is fractured, exposing the pulp, it may be uninfected, but if the pulp remains open to mouth fluids, organisms soon become implanted in the pulp chamber, when the condition resembles that of a carious exposure.

As a result of the invasion of organisms into the pulp tissue, the inevitable response of the tissues to infection occurs, and the phenomenon of inflammation is produced.

Polymorphonuclear leucocytes make their way from the neighbouring vessels to the site of the infection, to be followed later by lymphocytes, or round cells. As a result of the inflammatory exudate, the organisms are pinned down to a small area and their further extension checked.

But for the fact that the area of infection is surrounded by patent dentinal tubules into which the organisms can grow, there is little doubt but that the leucocytes would succeed in destroying the invaders, once the carious cavity was cleaned and filled. As it is, the organisms persist, and a chronic abscess is formed opposite the exposure, but usually the lesion does not remain in this condition for long. Much more often the inflammatory condition of the pulp leads to stasis and death of the pulp. As a result of the phagocytosis and inflammatory exudate, the pulp tissue becomes congested, and it would seem probable that, owing to the swelling at the apical portion of the root, the vessels carrying away the waste products become compressed. Often the more resilient afferent vessels continue to pump blood into the already engorged canal, with the result that stasis and death of the pulp occur. The dentinal tubules then become filled with blood which gives the tooth the familiar blue shade which changes to brown as the hæmosiderin crystals coalesce. The organisms are able to grow at will amongst the dead tissue and it is only a matter of time before they reach the peri-apical tissues.

The lapse of time from the initial exposure to the final death of the pulp varies considerably, and depends upon the position of the exposure and its size, which governs the amount of inflammatory exudate which can escape. If the cavity is situated on the biting surface, pieces of food débris are likely to be bitten into the carious cavity, and organisms are pushed further into the pulp, with the formation of an acute abscess. This interval may vary from a day to several months or even years, but at its commencement the patient is usually fully conscious of the fact that there is a pulp exposure,

because of the exquisite pain which such a condition usually engenders. It is not surprising, then, that the patient at this stage seeks the aid of a dental surgeon, and if he decides to save the tooth it is left to his skill and judgment as to whether the final root-filled tooth will be healthy or not. Bearing in mind that the pulp canal is as yet uninfected, the whole aim of root canal treatment must be to see that organisms are not accidentally implanted there during root canal instrumentation. Any infection of the peri-apical tissues after removal of a vital pulp must be due to contamination during the operation, unless there is a leak in the crown filling.

There are four principal methods of treatment on teeth with exposed pulps: (1) Pulp capping. (2) Devitalizing the pulp by applying an escharotic such as arsenic. (3) Removing the pulp under pressure anæsthesia. (4) Removing the pulp under a local anæsthetic.

(1) As it is unlikely that the tissues remain uninfected when the pulp is exposed, no matter from what cause, it is obviously unwise to cover the pulp with a cap without first sterilizing the tissues underneath. The use of a powerful antiseptic causes destruction of tissue, whilst the drug can hardly be expected to destroy every organism present.

C   Carious exposure.   I   Localized inflammation surrounding the invading organisms.

Photomicrograph × 37 of a decalcified section of the pulp canal of a human incisor showing the reaction of the tissues to a carious exposure (C). There is a localized concentration of polymorphonuclear leucocytes and round cells surrounding the invading organisms in the pulp chamber (I).

A few years ago a series of experiments was carried out upon monkeys, in which the pulps were opened up under a general anæsthetic (Ross 1937). In order to simulate the conditions present in the human mouth when a pulp is exposed by a bur, no attempt was made to carry out the operation under strict aseptic conditions. After exposure, the pulp was touched with the actual cautery and a sterile pulp cap immediately placed in position and sealed with cement. The teeth were eventually stained, sectioned, and examined under the microscope. The results showed that the application of the cautery had destroyed the great majority of the organisms which would inevitably be present under these conditions. Unfortunately, the application of the cautery sometimes caused a severe inflammation of the pulp, with an accompanying risk of death of the organ, so that such a method of sterilizing the vital pulp was discontinued. The experiments did, however, open the way to further methods which will be described later.

Perhaps the only justification of using a pulp cap over an exposure is when it occurs in a young tooth in which the apex is still open. At a later date, the pulp can be extirpated, the root apex having closed in the meantime. Usually the pulp is found to have a chronic ulcer under a pulp cap, although the infection is often limited and gives no discomfort to the patient.

(2) A commonly used method is to devitalize the exposed pulp by the application of arsenic. The obvious advantages are that it can be applied simply and quickly and the arsenic can usually be relied upon to kill the pulp without undue pain. For some time, however, there has been some doubt as to whether the arsenic does actually destroy all the organisms present in the pulp chamber of a tooth with a carious exposure. Quite

recently a series of experiments was carried out in collaboration with Dr. Maclean, with a view to finding out whether, in fact, the root canals were sterile after the pulp had been killed by applying arsenic. Twenty-one typical cases of pulp exposure with accompanying toothache were chosen, and after cleaning out the carious cavity, the ordinary commercial arsenic fibre was inserted over the exposure and sealed with a sterile metal cap and zinc oxide and cloves. The arsenic fibre consisted of a mixture of arsenic, creosote, tannin and oil of cassia. The teeth were left for one week, and then extracted under sterile conditions, which included cauterizing the gingival sulcus. They were placed in sterile tubes, with the arsenic dressing still in place, and sent to be cultured. The teeth were first split and the pulp or pulp débris teased out with sterile barbed broaches and then incubated. In every case a heavy growth of *Streptococcus viridans* was grown after two days' incubation.

(3) In view of the histological findings that the exposed pulp shows a concentration of organisms in the pulp chamber opposite the exposure, the method of removing the pulp after pressure anæsthesia with cocaine pellets need only be mentioned to be condemned.

(4) Extirpation of the pulp under local anæsthesia is in common use amongst many dental surgeons, but it is at once obvious that the entry of a root canal instrument such

N Normal pulp tissue.

Further down the pulp canal the tissues remain normal and healthy (N). × 37.

as a barbed broach into the pulp canal with a view to extirpating the pulp must first pass through the infected mass lying under the exposure. During its passage to the apex the instrument contaminates the rest of the pulp tissue, which up to this time has remained normal and uninfected. Upon the pulp being extirpated, organisms are then sucked into the apical third of the root, where they become implanted in some of the many small blood clots which form in the accessory canals. As a result of this procedure, the operator has contaminated the apical third of the root, which has been shown to be a perfect nidus for organisms to grow in, out of harm's way from the cellular defences of the body.

In order to substantiate these findings a series of experiments was carried out with Dr. Rogers of St. Mary's Hospital (Ross, 1943). Patients complaining of acute toothache had first 10 c.c. of blood taken from the median basilic vein. In each case this sample was shown to be sterile. The patient was then anæsthetized, either by nitrous oxide, or by local injection, and a barbed broach inserted into the canal of the inflamed tooth with a view to extirpating the pulp, the operation following the lines of usual routine practice. Before eventually extracting the tooth, a further 10 c.c. of blood was taken, and this further sample was found to be infected with *Str. viridans*. Once these results had been obtained upon three separate cases, the experiment was discontinued, since it was not considered advisable to produce a bacteriæmia, however transient it might prove to be. The experiments have shown that it is possible to produce a bacterial shower into the blood-stream as a result of passing a barbed broach into the root canal of an exposed pulp. From this it follows that organisms would also become implanted in the apical canals of the tooth during the operation. From the foregoing experiments and conclusions, it will be readily understood that the fundamental principle underlying vital

because of the exquisite pain which such a condition usually engenders. It is not surprising, then, that the patient at this stage seeks the aid of a dental surgeon, and if he decides to save the tooth it is left to his skill and judgment as to whether the final root-filled tooth will be healthy or not. Bearing in mind that the pulp canal is as yet uninfected, the whole aim of root canal treatment must be to see that organisms are not accidentally implanted there during root canal instrumentation. Any infection of the peri-apical tissues after removal of a vital pulp must be due to contamination during the operation, unless there is a leak in the crown filling.

There are four principal methods of treatment on teeth with exposed pulps: (1) Pulp capping. (2) Devitalizing the pulp by applying an escharotic such as arsenic. (3) Removing the pulp under pressure anæsthesia. (4) Removing the pulp under a local anæsthetic.

(1) As it is unlikely that the tissues remain uninfected when the pulp is exposed, no matter from what cause, it is obviously unwise to cover the pulp with a cap without first sterilizing the tissues underneath. The use of a powerful antiseptic causes destruction of tissue, whilst the drug can hardly be expected to destroy every organism present.

C Carious exposure.   I Localized inflammation surrounding the invading organisms.

Photomicrograph × 37 of a decalcified section of the pulp canal of a human incisor showing the reaction of the tissues to a carious exposure (C). There is a localized concentration of polymorphonuclear leucocytes and round cells surrounding the invading organisms in the pulp chamber (I).

A few years ago a series of experiments was carried out upon monkeys, in which the pulps were opened up under a general anæsthetic (Ross 1937). In order to simulate the conditions present in the human mouth when a pulp is exposed by a bur, no attempt was made to carry out the operation under strict aseptic conditions. After exposure, the pulp was touched with the actual cautery and a sterile pulp cap immediately placed in position and sealed with cement. The teeth were eventually stained, sectioned, and examined under the microscope. The results showed that the application of the cautery had destroyed the great majority of the organisms which would inevitably be present under these conditions. Unfortunately the application of the cautery sometimes caused a severe inflammation of the pulp, with an accompanying risk of death of the organ, so that such a method of sterilizing the vital pulp was discontinued. The experiments did, however, open the way to further methods which will be described later.

Perhaps the only justification of using a pulp cap over an exposure is when it occurs in a young tooth in which the apex is still open. At a later date, the pulp can be extirpated, the root apex having closed in the meantime. Usually the pulp is found to have a chronic ulcer under a pulp cap, although the infection is often limited and gives no discomfort to the patient.

(2) A commonly used method is to devitalize the exposed pulp by the application of arsenic. The obvious advantages are that it can be applied simply and quickly and the arsenic can usually be relied upon to kill the pulp without undue pain. For some time, however, there has been some doubt as to whether the arsenic does actually destroy all the organisms present in the pulp chamber of a tooth with a carious exposure. Quite

recently a series of experiments was carried out in collaboration with Dr. Maclean, with a view to finding out whether, in fact, the root canals were sterile after the pulp had been killed by applying arsenic. Twenty-one typical cases of pulp exposure with accompanying toothache were chosen, and after cleaning out the carious cavity, the ordinary commercial arsenic fibre was inserted over the exposure and sealed with a sterile metal cap and zinc oxide and cloves. The arsenic fibre consisted of a mixture of arsenic, creosote, tannin and oil of cassia. The teeth were left for one week, and then extracted under sterile conditions, which included cauterizing the gingival sulcus. They were placed in sterile tubes, with the arsenic dressing still in place, and sent to be cultured. The teeth were first split and the pulp or pulp débris teased out with sterile barbed broaches and then incubated. In every case a heavy growth of *Streptococcus viridans* was grown after two days' incubation.

(3) In view of the histological findings that the exposed pulp shows a concentration of organisms in the pulp chamber opposite the exposure, the method of removing the pulp after pressure anæsthesia with cocaine pellets need only be mentioned to be condemned.

(4) Extirpation of the pulp under local anæsthesia is in common use amongst many dental surgeons, but it is at once obvious that the entry of a root canal instrument such

N   Normal pulp tissue.

Further down the pulp canal the tissues remain normal and healthy (N).   × 37.

as a barbed broach into the pulp canal with a view to extirpating the pulp must first pass through the infected mass lying under the exposure. During its passage to the apex the instrument contaminates the rest of the pulp tissue, which up to this time has remained normal and uninfected. Upon the pulp being extirpated, organisms are then sucked into the apical third of the root, where they become implanted in some of the many small blood clots which form in the accessory canals. As a result of this procedure, the operator has contaminated the apical third of the root, which has been shown to be a perfect nidus for organisms to grow in, out of harm's way from the cellular defences of the body.

In order to substantiate these findings a series of experiments was carried out with Dr. Rogers of St. Mary's Hospital (Ross, 1943). Patients complaining of acute toothache had first 10 c.c. of blood taken from the median basilic vein. In each case this sample was shown to be sterile. The patient was then anæsthetized, either by nitrous oxide, or by local injection, and a barbed broach inserted into the canal of the inflamed tooth with a view to extirpating the pulp, the operation following the lines of usual routine practice. Before eventually extracting the tooth, a further 10 c.c. of blood was taken, and this further sample was found to be infected with *Str. viridans*. Once these results had been obtained upon three separate cases, the experiment was discontinued, since it was not considered advisable to produce a bacteriæmia, however transient it might prove to be. The experiments have shown that it is possible to produce a bacterial shower into the blood-stream as a result of passing a barbed broach into the root canal of an exposed pulp. From this it follows that organisms would also become implanted in the apical canals of the tooth during the operation. From the foregoing experiments and conclusions, it will be readily understood that the fundamental principle underlying vital

pulp extirpation is to destroy organisms already ensconced in the pulp chamber before any attempt is made to pass cold instruments into the root canal.

The method about to be described makes use of two electrically heated instruments, which it is believed are capable of destroying bacteria in the carious cavity and in the pulp, the electric cautery which is sufficiently well known to need no explanation, and the root desiccator. The latter is an instrument designed on the lines of the ordinary root canal drier, which is fitted to most modern dental units. For this purpose, however, a heavy current is needed, in order to heat the metal point to a temperature which will burn or incinerate the contents of the pulp, and in so doing, destroy the bacteria present. Perhaps the best example is an instrument which was designed for Dr. Fish, and is made up on robust ebony handles, and can be plugged into a flex lead which connects up with a transformer, giving six volts at fourteen amps. from the main current. A heavy foot switch operated by a spring which cuts off the current on being released is connected in series with the primary windings of the transformer. This type of switch has been found preferable to the type which is incorporated in the handle of the instrument, such as the root drier, and which for convenience has to be made of delicate structure, and when using a heavy current, frequently becomes hot and burns out. After inducing local anæsthesia, preferably by intra-osseous injection, the tooth to be operated on should be isolated from mouth fluids by means of cotton-wool pads or rubber dam. All burs and instruments should be boiled immediately before use and laid in spirit. A few drops of an antiseptic such as one of the formalin-cresol preparations are poured into a dappen glass and placed close to the operator. Every instrument before being introduced into the mouth should be dipped into the formalin solution first, in order to eliminate the risk of chance infection.

Enamel edges are chiselled away, and gross caries carefully removed with a large rose-head bur. Care must be taken to prevent any pressure reaching the exposed pulp, since this might be the cause of introducing fresh organisms into the pulp vessels. At this stage the cavity should be cauterized with the ordinary electric cautery. The cavity is opened up further to allow of easy access to the pulp chamber, the exposure widened, and the area cauterized again. The cavity is well soaked with formalin and the electric pulp desiccator then introduced into the pulp chamber, care being taken to see that it is already hot before application. The instrument is passed very slowly along the root canal, burning the pulp tissue as it progresses towards the apex. The length of time this operation takes will depend on the temperature of the instrument, but as an indication of this, the operator should be able to feel the external surface of the crown of the tooth becoming hot to the finger, and may see the contents of the pulp boiling during the procedure. Formalin is now introduced into the canal by means of a smooth broach and cotton-wool dipped in the antiseptic. When the canal is thoroughly saturated with the solution, the root desiccator is passed into the canal for a second time, and kept there until the formalin boils off. The canal is again filled with formalin, enlarged by suitable root reamers, and immediately filled with an adequate impermeable filling.

CONCLUSIONS

In practically all cases of pulp exposure there is a localized infection in the pulp chamber. The passage of a cold instrument along the root canal with a view to extirpating the pulp passes through the infected mass and contaminates the rest of the pulp tissue. This is considered to be the principal cause of apical infection following the removal of a vital pulp.

The use of arsenic as a method of devitalizing the pulp does not appear to destroy all the organisms which are present in a pulp with a carious exposure, with the result that apical infection occurs.

In addition there is often widespread destruction of the peri-apical tissues as a result of the use of arsenic, and this damaged area offers an additional nidus for the growth of organisms.

The first essential in root canal therapy must be to destroy organisms situated in the pulp chamber before any attempt is made to kill or extirpate the pulp. This can be carried out by the use of cautery and desiccator as described in the text.

REFERENCES

ROSS, W. STEWART (1037) *Brit. Dent. J.*, 63, 337.
—— and ROGERS, KEITH (1943) *Brit. Dent. J.*, 74, 253.

Some Aspects of Dentistry in relation to Aviation

By Squadron Leader WARREN HARVEY

[A BRIEF introduction described events occurring in the development of aviation from the eighteenth century (Hodgson, 1924) with particular reference to such phenomena as pain in the ears, and the effects of oxygen lack, which presaged the link of aviation with medicine, and later with dentistry (Neblett, 1923).]

Much experimental work and the training and testing of air crews can be done in a decompression chamber (fig. 1). This chamber has entrance doors at either end and is
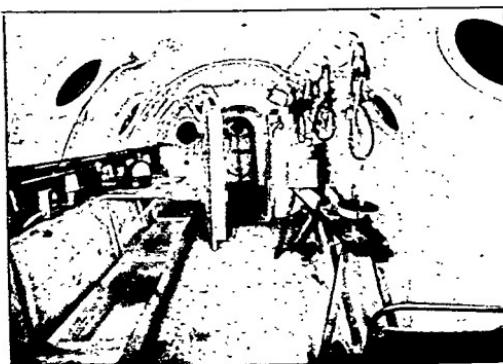
FIG. 1.

divided into two compartments separated by double bulkhead doors; the air is exhausted by a vacuum pump and oxygen is supplied at numerous points to which oxygen masks can be connected; some decompression chambers can also be refrigerated and excessive ventilation can produce a draught.

Mobile decompression chambers are available for outlying stations.

CHANGE IN TEMPERATURE

During ascent the air becomes less dense and there may be insufficient oxygen in the inspired air to maintain efficiency or even life. A method of supplying oxygen is shown in fig. 2, which is but a slight modification of the method used by Tissandier and his

FIG. 2.

companions in 1875 (Glaisher, 1875). The temperature decreases about 2° C. for every 1,000 feet ascended, thus, a jet of extremely cold oxygen may issue from the pipe stem mouthpiece and impinge on the teeth or mucous membranes; frost-bite of the cheek from this cause has been described, so that with this equipment cold might well be an important factor in the production of dental pain while flying.

pulp extirpation is to destroy organisms already ensconced in the pulp chamber before any attempt is made to pass cold instruments into the root canal.

The method about to be described makes use of two electrically heated instruments, which it is believed are capable of destroying bacteria in the carious cavity and in the pulp, the electric cautery which is sufficiently well known to need no explanation, and the root desiccator. The latter is an instrument designed on the lines of the ordinary root canal drier, which is fitted to most modern dental units. For this purpose, however, a heavy current is needed, in order to heat the metal point to a temperature which will burn or incinerate the contents of the pulp, and in so doing, destroy the bacteria present. Perhaps the best example is an instrument which was designed for Dr. Fish, and is made up on robust ebony handles, and can be plugged into a flex lead which connects up with a transformer, giving six volts at fourteen amps. from the main current. A heavy foot switch operated by a spring which cuts off the current on being released is connected in series with the primary windings of the transformer. This type of switch has been found preferable to the type which is incorporated in the handle of the instrument, such as the root drier, and which for convenience has to be made of delicate structure, and when using a heavy current, frequently becomes hot and burns out. After inducing local anæsthesia, preferably by intra-osseous injection, the tooth to be operated on should be isolated from mouth fluids by means of cotton-wool pads or rubber dam. All burs and instruments should be boiled immediately before use and laid in spirit. A few drops of an antiseptic such as one of the formalin-cresol preparations are poured into a dappen glass and placed close to the operator. Every instrument before being introduced into the mouth should be dipped into the formalin solution first, in order to eliminate the risk of chance infection.

Enamel edges are chiselled away, and gross caries carefully removed with a large rose-head bur. Care must be taken to prevent any pressure reaching the exposed pulp, since this might be the cause of introducing fresh organisms into the pulp vessels. At this stage the cavity should be cauterized with the ordinary electric cautery. The cavity is opened up further to allow of easy access to the pulp chamber, the exposure widened, and the area cauterized again. The cavity is well soaked with formalin and the electric pulp desiccator then introduced into the pulp chamber, care being taken to see that it is already hot before application. The instrument is passed very slowly along the root canal, burning the pulp tissue as it progresses towards the apex. The length of time this operation takes will depend on the temperature of the instrument, but as an indication of this, the operator should be able to feel the external surface of the crown of the tooth becoming hot to the finger, and may see the contents of the pulp boiling during the procedure. Formalin is now introduced into the canal by means of a smooth broach and cotton-wool dipped in the antiseptic. When the canal is thoroughly saturated with the solution, the root desiccator is passed into the canal for a second time, and kept there until the formalin boils off. The canal is again filled with formalin, enlarged by suitable root reamers, and immediately filled with an adequate impermeable filling.

CONCLUSIONS

In practically all cases of pulp exposure there is a localized infection in the pulp chamber. The passage of a cold instrument along the root canal with a view to extirpating the pulp passes through the infected mass and contaminates the rest of the pulp tissue. This is considered to be the principal cause of apical infection following the removal of a vital pulp.

The use of arsenic as a method of devitalizing the pulp does not appear to destroy all the organisms which are present in a pulp with a carious exposure, with the result that apical infection occurs.

In addition there is often widespread destruction of the peri-apical tissues as a result of the use of arsenic, and this damaged area offers an additional nidus for the growth of organisms.

The first essential in root canal therapy must be to destroy organisms situated in the pulp chamber before any attempt is made to kill or extirpate the pulp. This can be carried out by the use of cautery and desiccator as described in the text.

REFERENCES

ROSS, W. STEWART (1937) *Brit. Dent. J.*, 63, 337.
—— and ROGERS, KEITH (1943) *Brit. Dent. J.*, 74, 253.
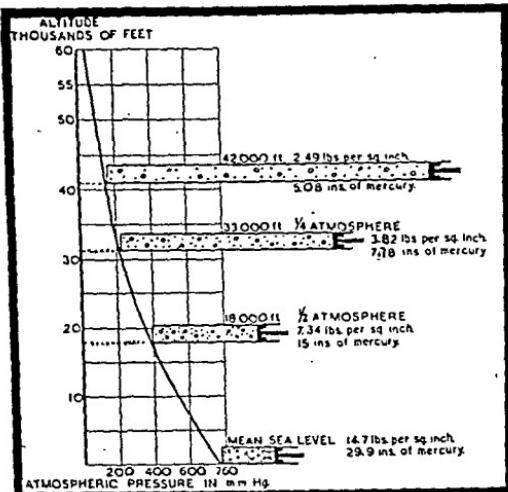
FIG. 4.

FIG. 5.

It has been suggested (Joseph, Gell, Carr, Shelesnyak, 1943, and others) that dental pain while flying may be caused in a filled tooth by the expansion of air entrapped while inserting the filling, so that pressure is exerted on the pulp via the dentinal tubules.

It was considered most unlikely that any significant volume of air was trapped while inserting the cement and amalgam or silicate or inlay, although there is no denying that pressure, even with cotton-wool, on a nearly exposed pulp can cause pain. But in order to disprove this theory, a deep occlusal inlay cavity was cut in a sound instanding upper premolar which was to be extracted to prevent the subsequent development of parodontal trouble. The radiograph in lower left hand corner of fig. 6 shows a copper wire inserted into a cornu of the pulp of the extracted tooth. Pain could not be elicited by pressure with an instrument in the cavity. The inlay was cast and a hole drilled through the centre; a copper capillary tube was inserted through the hole and soldered in position. One millimetre was stoned off the base of the inlay and tube so that a large space remained between the inlay and floor of the cavity when the inlay was carefully cemented in. The capillary tubing was connected to a sphygmomanometer and the pressure was increased to 300 mm. of mercury; five minutes later the patient noticed a throbbing pain which was relieved by reducing the pressure; thus a maintained pressure of 300 mm. of mercury in a sound cavity can produce pain. The sphygmomanometer was removed and the copper tube sealed so that a relatively large volume of air remained in communi-

Fortunately the modern type of oxygen equipment includes a face mask so that the oxygen is dispersed before inhalation (fig. 3).

FIG. 3.

These changes in temperature while flying may cause dental pain or have a deleterious effect on fillings. Armstrong and Huber in America observed in 1937 that temperatures of 0 to $-50°$ C. had no effect on sound and filled extracted teeth. Freitag in Germany confirmed this work in 1942.

However, since both these observations concerned extracted teeth and it was doubted whether there was any great change in tooth temperature while flying, it was considered advisable to measure the temperature of vital teeth under various conditions (Harvey, 1942).

An oxygen mask was fitted with six small copper constantan thermocouples: some of these couples were inserted into cavities prepared in vital teeth and sealed in with gutta-percha, amalgam being used for one case. The current from the thermocouples was balanced by a secondary circuit controlled by a potential divider to give a null reading on the galvanometer. The reading of the potential divided was calibrated against known temperatures.

Under the varying conditions of (i) oral and nasal breathing, (ii) intermittent and constant oxygen flow, (iii) still air and a draught, (iv) with and without a heater element in the mask, tooth temperature at various positions in the mouth did not drop below $20°$ C.; pain only occurred when iced water reduced the tooth temperature to $12°$ C. These results are supported by the fact that men in the coldest aircraft or the most exposed positions are not those who complain most frequently of dental pain while flying.

Several workers have observed the temperature of extracted teeth during drilling and so the opportunity was taken of determining the temperature produced in a vital tooth while a large amalgam filling was being drilled out: unless suitable precautions are taken, the heat may be quite sufficient to cause a burn of the pulp, so that the heat produced while burring may be much more deleterious to the pulp than the cold conditions of flying.

CHANGE IN GAS VOLUME

Change in gas volume is the second condition occurring during ascent which may have a relation to dental pain while flying.

It may be considered that the gases in the body will obey Boyle's law so that at a pressure of ½ an atmosphere at 18,000 feet the original volume is doubled, it is quadrupled at 32,000 feet and six times its original volume at 42,000 feet (fig. 4).

Gas in the root canal of a putrescent pulp will behave similarly and a radiograph of a case where this was probably the cause of pain while flying was shown.

It has been reported (Stewart and MacIntosh, 1943) that apical areas might "flare up" and cause swelling at altitude and become painful—though how this can occur is not clear. The X-rays shown in fig. 5 were taken in a decompression chamber at ground level (A) and 40,000 feet (B); there may possibly be less peripheral definition of the area at altitude—though this may be due to the slight variation in the angulation of the patient. This man had no pain at altitude. Cases have been seen, however, where an apical infection has developed into an acute abscess after decompression.

It will be seen that there is no significant difference between the failures and the controls. During the decompression tests on 1,000 men there were only 89 cases which developed symptoms in their ears. When decompressed three times there were only 7 men out of these 89 who had pain on each occasion; of these 7 men there were only 3 men (i.e. 3 out of 1,000) whose otorhinolaryngological history offered no possible contributory factors, and in one of these men malocclusion may have been a factor—he had an Angle Class 2, division 1 type of occlusion.

Seven men were chosen who had failed on two or more occasions in the decompression chamber and who had overclosure of the mandible. Small softened composition blocks on a palatal arch wire were inserted in the mouth so that there was an open bite of 0·5 cm. in the incisor region (this opening was greater than that used in many of the cases reported in the literature). X-rays of left and right temporomandibular joints were taken with the teeth in centric occlusion, with the blocks in position and with the jaws fully opened. The men were decompressed again with the blocks in position and only, 3 of the 7 had no pain—and all of these 3 had had colds on previous tests. The man who had the worst overclosure had no pain but he had passed on one previous occasion without the blocks in position!

The X-rays are shown in fig. 7 of one man who failed on two tests, passed on the
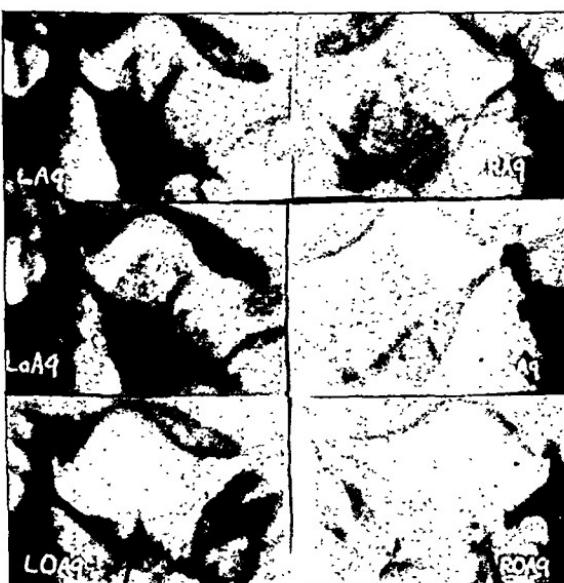
FIG. 7.

third, but failed on the fourth test with the blocks in position; his occlusion was Angle Class 2, division 1.

It is concluded then that overclosure of the mandible may be a factor in preventing successful ventilation of the middle ear, but it is a very rare cause. The blocks seriously interfered with intercommunication and some cases found it difficult to swallow with the bite opened.

GAS IN SOLUTION

The third change due to altitude, which may have a dental significance, is that affecting gas in solution.

In soda water carbon dioxide is present under pressure in solution, so that when the tap is pressed and the pressure is reduced the dissolved gas in the released liquid is no longer held in solution and bubbles begin to form.

Normally the blood and tissues at ground level are saturated with nitrogen so that when the pressure is reduced during ascent, there may come a time when the nitrogen is no longer held in solution and bubbles appear in the tissues and the blood.
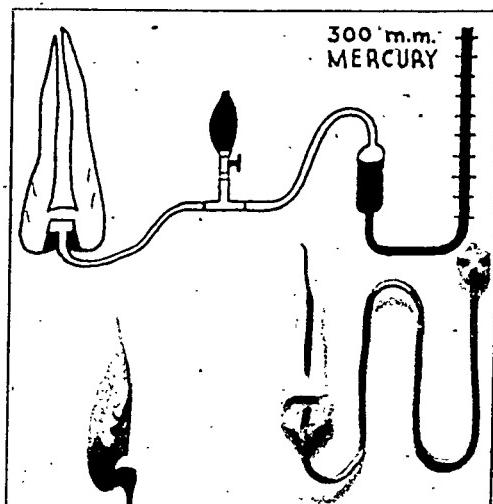
FIG. 6.

cation with the dentinal tubules. The patient was then decompressed to 25,000 feet for ten minutes and no pain was experienced; the change in pressure from ground level to 25,000 feet is +78 mm. of mercury.

It may be concluded that air under fillings is not a likely cause of dental pain while flying.

During ascent the air in the middle ear expands and escapes through the Eustachian tube, without usually causing any discomfort; during descent air has to be introduced into the middle ear ,to equalize the increasing pressure on the drum, and swallowing, Valsalva's manœuvre (blowing with nose and mouth closed), jaw movement or a combination of these methods may be used to assist the passage of air up the tubes.

During descent from 30,000 feet to 20,000 feet there is an increase in pressure of 2·3 lb. per square inch, but since air becomes denser during descent there is an increase of 4·3 lb. per square inch from 12,000 feet to 2,000 feet—so this pain in ears or otitic barotrauma is much commoner while diving at the lower altitudes (McGibbon, 1942a and b).

Much has been written in the last twenty years concerning the relation of the occlusion to impaired hearing in middle life. Willhelmy in 1936, Lowry in 1939 and Brickman and Bierman in 1943 state that overclosure of the mandible in aircrew age-groups is an important predisposing cause of otitic barotrauma or pain in the ears while flying. Beneficial results were said to follow opening the bite and repositioning the mandible. Unfortunately these reports contained no references to the otorhinolaryngological condition or to the history of the cases treated.

Through the courtesy and co-operation of the Consultant in Otorhinolaryngology to the Royal Air Force, Air Commodore Dickson, and his Staff, an investigation has recently been concluded into the dental aspects of otitic barotrauma. There were 50 cases of acute otitic barotrauma while decompressing 690 men; these men were dentally inspected together with an equal number of men who were decompressed but had no pain in their ears, and the results are shown in Table I (Dickson, McGibbon, Harvey, Turner, 1943).

TABLE I.—OTITIC BAROTRAUMA AND MALOCCLUSION.

Results.—There were 50 cases of acute otitic barotrauma while decompressing 690 subjects, i.e. an incidence of 7·2%. Analysis of 50 subjects who developed acute otitic barotrauma and of 50 control subjects.

				Subjects who developed acute otitic barotrauma (50)	Control subjects (50)
Normal occlusion	...	...	...	12%	16%
Angle's Class 1	...	...	...	48%	44%
Angle's Class 2	...	...	...	22%	28%
Angle's Class 3	...	...	...	18%	12%
Incisal overclosure	...	...	...	42% of which:	48% of which:
				9% +++	00% +++
				34% ++	25% ++
				48% +	48% +
				9% mild	27% mild
Total number of teeth missing	...			266	283
Number of molars missing	...			131	121
Colds...	...	...	...	78%	40%
Average age in years				21	19

Assuming that the two groups are representative of cases and controls, the percentage of 690 cadets who developed acute otitic barotrauma are: with normal occlusion=5·6%; with malocclusion=7·5%.

Section of Odontology

Under local anæsthesia, control teeth were removed at ground level, and using a modified nasal oxygen mask, teeth were removed, using novocain epinephrine again at varying altitudes up to 40,000 feet; the apices were removed and the teeth were placed in 10% formol saline at altitude.

Photomicrographs are shown in fig. 10 from the central group of serial sections of the
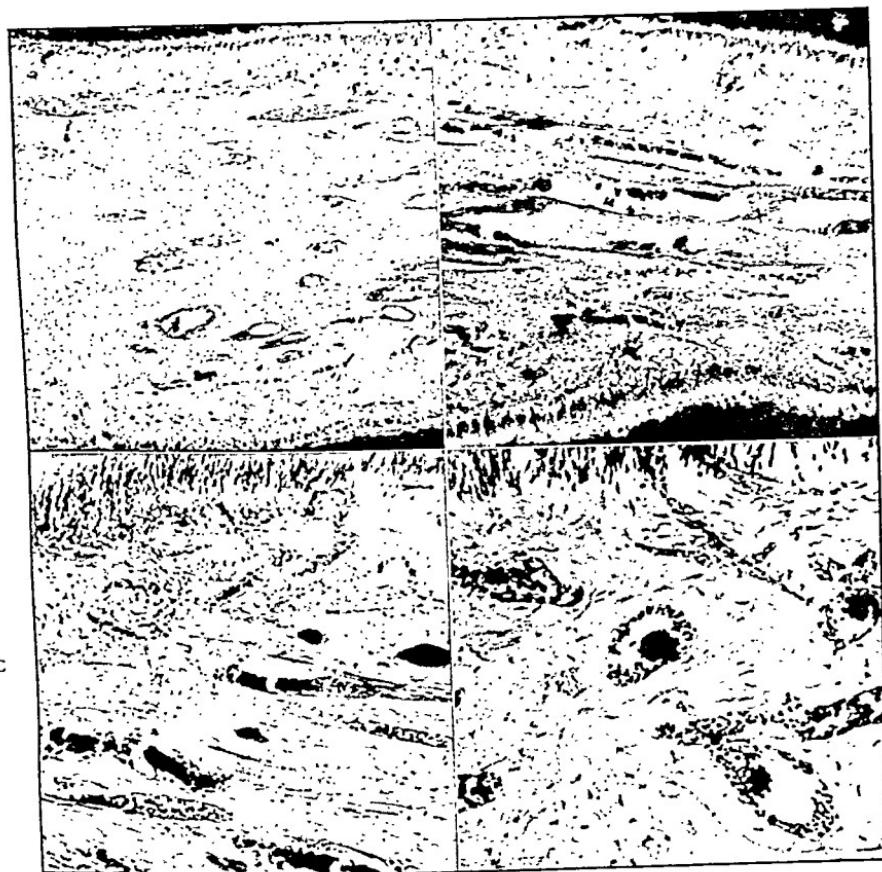
FIG. 10.

pulp of an incisor (A) extracted at ground level and a canine (B, C, D) extracted at 35,000 feet. The magnifications are A × 40, B × 45, C × 80, D × 135.

The patient was aged 24 and had no symptoms of anoxia. He showed signs of interest rather than apprehension. (A similar series of photomicrographs were shown of a canine extracted at ground level compared with an incisor extracted at altitude.)

The changes in the capillaries of the nail-bed occurring at ground level and altitude are suggestive but not conclusive—cine photomicrographs or a continuous record of any volume changes are really necessary.

The photomicrographs in fig. 11 show the skin capillaries at ground level (A) and after half an hour at 35,000 feet (B). The skin was kept at constant temperature throughout the experiment.

Inflammation of the pulp may be insufficient to cause symptoms unless certain provocative conditions occur; the pain which occurs when a patient lies down in bed is probably due to the change in local pressure which occurs with the recumbent position and the peripheral vasodilatation which is said to occur prior to sleep acting on what was a subclinical pulpitis. Then there is the story of the lady who confessed that she had toothache only when a particular nephew kissed her! Emotion can cause a marked vasodilatation and if there is a pre-existing inflammation in a tissue enclosed by rigid walls, then the stage is set for the production of pain.

Fig. 8 is a picture of bubbles in the veins of an animal after decompression—they would of course be much larger at altitude. Bubbles may also be found in end arteries, resulting in an area of ischæmia beyond the bubble (Armstrong, 1939).

FIG. 8.—Reproduced from " Principles and Practice of Aviation Medicine,"
by H. G. Armstrong, 1939. Baltimore and London.

Similar effects may occur while divers are being decompressed or brought to the surface and may cause various symptoms such as pain in the limbs or paralysis—known as "bends".

Fig. 9 is an X-ray of a patient who had been a deep sea diver and had been endentulous

FIG. 9.

for many years; suppuration started spontaneously in the mandible and lasted for about a year until the sequestrum was removed. Recovery was uneventful, and he has passed his medical test for further deep sea diving! (Eckhoff, 1943.) Caisson disease has been described as causing an aseptic necrosis of the humeri (Swain, 1942) and this may be a case of caisson disease or "bends" of the jaw.

Fortunately such delayed effects are unknown in airmen and the results of decompression sickness have usually disappeared before ground level is reached. Although proof is extremely difficult to produce, the author knows of no reason why teeth should not be subject to the same changes due to altitude as the rest of the body.

VASCULAR CHANGE

There have been various references (Kniseley, 1943, and others) to a fourth effect of altitude on the body—a vascular change. In order to study this in dental tissues, 23 men of several age-groups were selected who were to have teeth extracted which were sound, but out of alignment, and which were to be extracted for parodontal reasons.

meter or by using indicators whose colours change over varying pH ranges. A pH above 7 is alkaline and below 7 is acid.

Using a glass electrode pH meter the acidity of 92 oxyphosphate and silicate cements was found to be below pH 2 at the time of insertion into the cavity (Harvey, Le Brocq and Rakowski, 1943); it should be noted that formic acid of this pH is used in some histological techniques to decalcify teeth.

A lining of zinc oxide with eugenol or clove oil gives complete protection against these acid cements. The addition of zinc acetate as a hastening agent to these mixtures has been undergoing Service trials for the past six months.

CENTRIFUGAL FORCE

The fifth effect of flying on the body which may produce dental symptoms is centrifugal force.

Centrifugal force is proportional to the square of the velocity and inversely proportional to the radius and is measured in units of gravity or G—thus the same G may be produced by a tight turn at a slow speed or a wide turn at a high speed.

Centrifugal force is obviously also a factor in looping and diving.

During a loop the blood tends to pool in the abdomen and limbs so that vision or even consciousness may be temporarily impaired or lost because of the fall of blood-pressure locally due to positive G. If the pilot goes into a sudden steep dive blood will tend to pool in his head and instead of vision blacking out the pilot may redden out due to the suffusion of the retina with blood caused by negative G, and this may produce conjunctival and other hæmorrhages.

When level flight is resumed after experiencing positive G there may be a temporary surge of blood to the head causing a pressure above normal. There are records of cases where dental pain occurred on going into and pulling out of a dive, and obviously all that has been said about an existing mild pulpitis applies here.

At 5G the blood may be as heavy as molten iron and a 12-stone man may weigh well over a third of a ton. Thus a full upper acrylic denture may weigh more than a quarter of a pound, and a large vulcanite denture more than half a pound when the pilot is exposed to a centrifugal force of 5G.

It is only just possible to raise one's arm at 5G and the facial features are dragged down as shown in fig. 12B. A colleague of the author's was asked early in the war by a pilot to make a denture which would stay put in a dive!

A
Level Flight.

B
Passenger subjected to 5G.

FIG. 12.

A series of radiographs were then shown of cases of dental pain which occurred while flying or in a decompression chamber. These cases were selected from centralized reports of pain occurring in men engaged in all types of flying, and included cases of impacted teeth, primary caries, recently filled teeth (lined and unlined), a dental cyst, chronic apical abscesses and root-filled teeth.

(This paper was illustrated with 38 slides.)

Fig. 8 is a picture of bubbles in the veins of an animal after decompression—they would of course be much larger at altitude. Bubbles may also be found in end arteries, resulting in an area of ischæmia beyond the bubble (Armstrong, 1939).

FIG. 8.—Reproduced from " Principles and Practice of Aviation Medicine," by H. G. Armstrong, 1939. Baltimore and London.

Similar effects may occur while divers are being decompressed or brought to the surface and may cause various symptoms such as pain in the limbs or paralysis—known as "bends".

Fig. 9 is an X-ray of a patient who had been a deep sea diver and had been endentulous

FIG. 9.

for many years; suppuration started spontaneously in the mandible and lasted for about a year until the sequestrum was removed. Recovery was uneventful, and he has passed his medical test for further deep sea diving! (Eckhoff, 1943.) Caisson disease has been described as causing an aseptic necrosis of the humeri (Swain, 1942) and this may be a case of caisson disease or "bends" of the jaw.

Fortunately such delayed effects are unknown in airmen and the results of decompression sickness have usually disappeared before ground level is reached. Although proof is extremely difficult to produce, the author knows of no reason why teeth should not be subject to the same changes due to altitude as the rest of the body.

VASCULAR CHANGE

There have been various references (Kniseley, 1943, and others) to a fourth effect of altitude on the body—a vascular change. In order to study this in dental tissues, 23 men of several age-groups were selected who were to have teeth extracted which were sound, but out of alignment, and which were to be extracted for parodontal reasons.

meter or by using indicators whose colours change over varying pH ranges. A pH above 7 is alkaline and below 7 is acid.

Using a glass electrode pH meter the acidity of 92 oxyphosphate and silicate cements was found to be below pH 2 at the time of insertion into the cavity (Harvey, Le Brocq and Rakowski, 1943); it should be noted that formic acid of this pH is used in some histological techniques to decalcify teeth.

A lining of zinc oxide with eugenol or clove oil gives complete protection against these acid cements. The addition of zinc acetate as a hastening agent to these mixtures has been undergoing Service trials for the past six months.

CENTRIFUGAL FORCE

The fifth effect of flying on the body which may produce dental symptoms is centrifugal force.

Centrifugal force is proportional to the square of the velocity and inversely proportional to the radius and is measured in units of gravity or G—thus the same G may be produced by a tight turn at a slow speed or a wide turn at a high speed.

Centrifugal force is obviously also a factor in looping and diving.

During a loop the blood tends to pool in the abdomen and limbs so that vision or even consciousness may be temporarily impaired or lost because of the fall of blood-pressure locally due to positive G. If the pilot goes into a sudden steep dive blood will tend to pool in his head and instead of vision blacking out the pilot may redden out due to the suffusion of the retina with blood caused by negative G, and this may produce conjunctival and other hæmorrhages.

When level flight is resumed after experiencing positive G there may be a temporary surge of blood to the head causing a pressure above normal. There are records of cases where dental pain occurred on going into and pulling out of a dive, and obviously all that has been said about an existing mild pulpitis applies here.

At 5G the blood may be as heavy as molten iron and a 12-stone man may weigh well over a third of a ton. Thus a full upper acrylic denture may weigh more than a quarter of a pound, and a large vulcanite denture more than half a pound when the pilot is exposed to a centrifugal force of 5G.

It is only just possible to raise one's arm at 5G and the facial features are dragged down as shown in fig. 12B. A colleague of the author's was asked early in the war by a pilot to make a denture which would stay put in a dive!

A   B
Level Flight.   Passenger subjected to 5G.
FIG. 12.

A series of radiographs were then shown of cases of dental pain which occurred while flying or in a decompression chamber. These cases were selected from centralized reports of pain occurring in men engaged in all types of flying, and included cases of impacted teeth, primary caries, recently filled teeth (lined and unlined), a dental cyst, chronic apical abscesses and root-filled teeth.

(This paper was illustrated with 38 slides.)

FIG. 1.

NOSEPIECE N. PERFORATED WITH AIR HOLES FOR RESPIRATION

"SPILLER TAP" USED IF WEAKER MIXTURE REQUIRED

BOTTLE J

LIQUID TRILENE

B. BULB B

AIR ENTERS BULB.

FIG. 2.

FIG. 3.

TRILENE CONCENTRATION
GRAMMES PER LITRE MIXTURE

WITH CONTROL VALVE SHUT

WITH CONTROL VALVE OPEN TO ATMOSPHERE

AIR PUMPED OVER WICK
IN LITRES/ MINUTE

FIG. 1.—Diagrammatic sketch of apparatus for the production of analgesia by self-administered trichlorethylene.

FIG. 2.—The apparatus shown in position for dental analgesia.

FIG. 3.—Graph showing output of trilene by apparatus.

subject spoke or commented upon any point, the breath following such an interruption was sometimes slightly irritant. During induction a sensation of general warmth and well-being was constantly observed with tingling sensations in the limbs, face and scalp. A noticeable sensation of "stiffness" of the facial muscles and the muscles of the tongue occurred frequently. After an interval of approximately thirty to sixty seconds from the beginning of induction it was common for a feeling of great drowsiness to arise and in this period there was a tendency for the squeezing of the bulb to be interrupted. The squeezing was invariably resumed, however, upon a word of encouragement from the observer. After a period of about one and a half to two minutes speech became thick and slow and a tendency to "lolling" of the head was noted. During some experiments the squeezing of the bulb ceased for periods up to three-quarters of a minute in duration but was in each case resumed spontaneously. The ability to phonate and to cough was never lost and deglutition was not impaired. No increase in salivation was observed. Although the experiments were carried out in a warm room it was a frequent occurrence for the subject to complain of "feeling chilly" upon their conclusion. Following periods of analgesia up to twenty minutes' duration, recovery was rapid, being complete within two minutes even after the longest experiments. Beyond a mild feeling of drowsiness which was fairly constant, no after-effects of any kind were observed.

Sensory and other tests carried out under trilene analgesia.—During the investigations tests of skin sensation were applied. In addition tests of powers of recognition and of memory were performed. By the application of either the sharp point or the blunt head of a pin to the hair-free skin of the forearm it was observed that the ability to

Trilene Auto-Analgesia

By Basil Hill, M.B., Ch.B., D.A.

ANALGESIA has been defined by McKesson (1935) as being a state in which pain is abolished without loss of consciousness occurring. Since this definition depends upon the implication of the word "consciousness" it would appear to be unsatisfactory. A more satisfactory definition was suggested by Hartridge in which he described analgesia as being a state in which the interpretation of the sense of pain is modified while that of the sense of touch may remain intact. Thus according to the latter definition analgesia differs from anæsthesia in which both senses are modified.

It has long been known that during the induction of anæsthesia of the general type there is a phase of general analgesia before the onset of the stage of complete oblivion. Wilson (1927) made a careful investigation of the analgesia associated with nitrous oxide anæsthesia and this gas is now widely used for the production of analgesia in dental surgery and in midwifery. Wilson referred to the difficulty which he experienced in arriving at the optimum mixture of nitrous oxide and air for the production of analgesia, and commented upon the wide variations in this mixture in different individuals and even in the same individual during one administration.

In a similar manner the analgesia produced by chloroform has been used extensively in midwifery and an apparatus for self-administered analgesia with this drug has been described by Mennell (1933). For general surgical and dental work chloroform analgesia has not been widely used, possibly owing to the toxicity of the drug.

Trichlorethylene ("trilene") as a general analgesic.—Hewer (1941) in an interim report upon the use of trilene as a general anæsthetic commented upon a phase of analgesia which was observed during the stage of induction. Again in 1942 Hewer reported this phase of analgesia to be almost consistently present although varying in intensity from some numbness to complete analgesia. He concluded that trichlorethylene was a more potent analgesic agent and at the same time less toxic agent than chloroform.

"Trilene", a stabilized preparation of trichlorethylene (CCl_2: CHCl) is a heavy non-inflammable liquid, only slightly volatile and possessing an odour somewhat resembling that of chloroform. In order to prevent its confusion with the latter drug, "trilene" is coloured blue. The liquid has good keeping qualities provided that it is properly stored.

An apparatus for the production of analgesia with self-administered "trilene".—By allowing the patient to administer "trilene" air mixture to himself with a simple apparatus it was found that an even level of useful analgesia could be obtained with safety. It was noted moreover that when once adequate analgesia had been established, it was easy for a patient to maintain the analgesia for periods up to twenty minutes without any further adjustment of the apparatus being required.

A rubber bulb, B (fig. 1), held in and squeezed by the hand of the patient propels air through a wick, W, saturated with trilene. The wick is enclosed in an amber-coloured bottle, J. The resulting trilene-air mixture is added to the air inspired by the patient through holes in a celluloid nosepiece, N. To avoid the possibility of the delivery of liquid trilene into the nosepiece, the bottle should be rendered unspillable, and incapable of having more than a few c.c. of liquid poured into it. With such an apparatus delivery of the vapour from the wick is made entirely dependent upon the ability of the patient to use the muscles necessary for the squeezing of the bulb. In the event of the stage of analgesia becoming too deep, the supply of vapour from the wick ceases, owing to cessation of the squeezing of the bulb. In order to minimize the possibility of the patient "drawing over" vapour from the wick by inspiratory effort, the air passages through the apparatus should be of narrow bore.

With such an apparatus, numerous experiments and tests were carried out by my wife (Dr. Betty F. Hill) and myself upon our own persons before the analgesia was applied clinically. Repeated attempts to produce full anæsthesia with the apparatus failed consistently and it was found that for short periods (up to twenty minutes) an even level of analgesia could be maintained without fatigue. Induction was pleasant. For the first few breaths the smell of the trilene was noticeable but it rapidly diminished so that after some twelve breaths it was not noticed. Provided that an even sequence of respirations was maintained during induction the vapour caused no irritation of the nasal passages. If, however, regular breathing was interrupted, as might occur if the

FIG. 1.

NOSEPIECE N. PERFORATED WITH AIR HOLES FOR RESPIRATION

"SPILLER TAP" USED IF WEAKER MIXTURE REQUIRED

W→

W→

W→

BOTTLE J

LIQUID TRILENE

B. BULB B

AIR ENTERS BULB.

FIG. 2.

FIG. 3.

0·3

TRILENE CONCENTRATION

0·2

GRAMMES PER LITRE MIXTURE

0·1

WITH CONTROL VALVE SHUT

WITH CONTROL VALVE OPEN TO ATMOSPHERE

AIR PUMPED OVER WICK

2   3   4   5

IN LITRES/ MINUTE

FIG. 1.—Diagrammatic sketch of apparatus for the production of analgesia by self-administered trichlorethylene.

FIG. 2.—The apparatus shown in position for dental analgesia.

FIG. 3.—Graph showing output of trilene by apparatus.

subject spoke or commented upon any point, the breath following such an interruption was sometimes slightly irritant. During induction a sensation of general warmth and well-being was constantly observed with tingling sensations in the limbs, face and scalp. A noticeable sensation of "stiffness" of the facial muscles and the muscles of the tongue occurred frequently. After an interval of approximately thirty to sixty seconds from the beginning of induction it was common for a feeling of great drowsiness to arise and in this period there was a tendency for the squeezing of the bulb to be interrupted. The squeezing was invariably resumed, however, upon a word of encouragement from the observer. After a period of about one and a half to two minutes speech became thick and slow and a tendency to "lolling" of the head was noted. During some experiments the squeezing of the bulb ceased for periods up to three-quarters of a minute in duration but was in each case resumed spontaneously. The ability to phonate and to cough was never lost and deglutition was not impaired. No increase in salivation was observed. Although the experiments were carried out in a warm room it was a frequent occurrence for the subject to complain of "feeling chilly" upon their conclusion. Following periods of analgesia up to twenty minutes' duration, recovery was rapid, being complete within two minutes even after the longest experiments. Beyond a mild feeling of drowsiness which was fairly constant, no after-effects of any kind were observed.

Sensory and other tests carried out under trilene analgesia.—During the investigations tests of skin sensation were applied. In addition tests of powers of recognition and of memory were performed. By the application of either the sharp point or the blunt head of a pin to the hair-free skin of the forearm it was observed that the ability to

discriminate between these stimuli remained almost unaffected under the analgesia. In the same manner the ability to discriminate between extremes of temperature was found to be perfect. It was observed, however, that although it was possible under the analgesia to discriminate between these stimuli, marked increase in the power of the stimulus did not give rise to a sensation of pain. Thus the mere resting of the point of the pin on the skin produced a sensation differing little from the sensation produced if the skin was penetrated by the point driven in by considerable pressure. In neither case was the stimulus appreciated as being painful, and reflex withdrawal was rarely observed. Recognition of familiar objects by the subject under analgesia was perfect, as was the recognition of familiar sounds and music. It was noted, however, that at the conclusion of the tests, memory of all events occurring during the test period had been very markedly impaired, and in certain cases obliterated. Thus the subject frequently failed to recall the objects and sounds placed before him while under analgesia, and on one occasion failed to remember whether any skin stimulation tests had been applied at all.

Being somewhat discouraged by the accuracy with which the skin stimuli had been recognized, we decided that similar comparative tests should be made under the analgesia of nitrous oxide delivered from a marketed apparatus. In the case of the analgesia produced by a mixture of this gas with air it was observed that a similar accuracy of discrimination was present but that the impairment of memory which had been so marked in the case of "trilene" was practically absent in the case of nitrous oxide-air analgesia.

Similar tests performed under the analgesia of chloroform self-administered by means of the Mennell apparatus demonstrated that the ability to discriminate between test stimuli applied to the skin remained almost intact, but that there was a well-marked degree of memory impairment. After-effects following the analgesia with this drug were more marked and took the form of nausea and headache.

From the above experiments it was concluded that the accuracy with which the skin stimuli had been recognized was in all probability dependent upon the sense of touch, which may not be altered by a state of analgesia, as opposed to the sense of pain interpretation which appeared to be markedly impaired in this state. It was also concluded that the state of analgesia produced by self-administered trilene compared most favourably with that induced with nitrous oxide and with chloroform and that certain disadvantages of the latter agents were absent in the case of trilene.

Clinical application.—Clinical application of the analgesia produced by self-administered trilene in patients undergoing painful procedures indicated that in the majority of such cases considerable alleviation of the pain occurred. Procedures such as the preparation of dental cavities, the removal of adherent dressings and wound suture were made tolerably comfortable to the patient, and were rendered completely painless in many cases. Moreover the almost constant impairment of memory which was associated with the analgesia tended towards the psychological comfort of the patient both during and following the operation.

Results obtained with "trilene" analgesia.—In 62 personally observed cases in which minor surgical procedures were carried out under the analgesia of "trilene", 27 cases experienced no pain whatsoever. In 11 of these cases wound suture had been carried out, and in 1 case drainage of an empyema was performed. In 27 cases discomfort, which according to the patient's own statement did not amount to pain, was complained of. In 8 cases the patients derived no benefit from the analgesia although in 6 of these cases there was no indication at the time that pain was being suffered. In 21 cases of the whole series memory of the procedure had been obliterated, impaired to some degree in 33, and had remained lucid in 8 cases.

Following this series of observed cases the apparatus was made available to the Nursing Staff of the Royal Berkshire Hospital for use in any case for which analgesia might seem indicated. The results have been satisfactory and no untoward effects have been seen over a large number of cases unsupervised by a medical practitioner.

With the kindly co-operation of Messrs. Guy Ellingham and P. H. Williams the application of self-administered analgesia with trilene in dental surgery was investigated over a considerable number of cases.

After-effects.—Few after-effects have been observed. In the series of observed cases one patient exhibited a state of confusion which resembled alcoholic intoxication. This persisted for about twenty minutes following which the patient was absolutely normal save for slight drowsiness. Dizziness was complained of in 17 cases, and its greatest duration was two hours. Nausea was observed in 3 cases but no case vomited.

SUMMARY AND CONCLUSIONS

The disadvantages of the analgesia produced by nitrous oxide and by chloroform have been mentioned and the possibility of using patient-administered trichlorethylene

FIG. 1.

NOSEPIECE N. PERFORATED WITH AIR HOLES FOR RESPIRATION

"SPILLER TAP" USED IF WEAKER MIXTURE REQUIRED

BOTTLE J

LIQUID TRILENE

W→
W→
W→

↑ B.
BULB B

AIR ENTERS BULB.

FIG. 2.

FIG. 3.

TRILENE CONCENTRATION — GRAMMES PER LITRE MIXTURE

WITH CONTROL VALVE SHUT

WITH CONTROL VALVE OPEN TO ATMOSPHERE

AIR PUMPED OVER WICK IN LITRES / MINUTE

0·3   0·2   0·1

2   3   4   5

FIG. 1.—Diagrammatic sketch of apparatus for the production of analgesia by self-administered trichlorethylene.

FIG. 2.—The apparatus shown in position for dental analgesia.

FIG. 3.—Graph showing output of trilene by apparatus.

subject spoke or commented upon any point, the breath following such an interruption was sometimes slightly irritant. During induction a sensation of general warmth and well-being was constantly observed with tingling sensations in the limbs, face and scalp. A noticeable sensation of "stiffness" of the facial muscles and the muscles of the tongue occurred frequently. After an interval of approximately thirty to sixty seconds from the beginning of induction it was common for a feeling of great drowsiness to arise and in this period there was a tendency for the squeezing of the bulb to be interrupted. The squeezing was invariably resumed, however, upon a word of encouragement from the observer. After a period of about one and a half to two minutes speech became thick and slow and a tendency to "lolling" of the head was noted. During some experiments the squeezing of the bulb ceased for periods up to three-quarters of a minute in duration but was in each case resumed spontaneously. The ability to phonate and to cough was never lost and deglutition was not impaired. No increase in salivation was observed. Although the experiments were carried out in a warm room it was a frequent occurrence for the subject to complain of "feeling chilly" upon their conclusion. Following periods of analgesia up to twenty minutes' duration, recovery was rapid, being complete within two minutes even after the longest experiments. Beyond a mild feeling of drowsiness which was fairly constant, no after-effects of any kind were observed.

Sensory and other tests carried out under trilene analgesia.—During the investigations tests of skin sensation were applied. In addition tests of powers of recognition and of memory were performed. By the application of either the sharp point or the blunt head of a pin to the hair-free skin of the forearm it was observed that the ability to

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*March* 24, 1944]

DISCUSSION ON PARENTERAL DIARRHŒA

Major T. F. McNair Scott, U.S.A.M.C.: The term parenteral diarrhœa connotes in the minds of pædiatricians diarrhœa associated with infection outside the alimentary tract. No definite pathology in the intestine itself can be found.

Diarrhœa has always been a major problem facing physicians in charge of children, particularly in the first two years of life. During the early part of the century it was a leading cause of death in infants under 2 years old, the main incidence occurring in the summer months. Investigation pointed to contaminated milk and poor hygiene as being the most important factors in this seasonal incidence and improvement in public health education and hygiene led to a decline of this summer diarrhœa. Although summer diarrhœa was of predominating importance, study of notifications reveals that a certain amount of diarrhœa occurred all through the year and that its incidence had not been lowered by the above measures. It was only when the incidence of summer diarrhœa fell below the level of this all-season diarrhœa, between 1920 and 1930, that the latter attracted attention. This residuum of diarrhœal diseases in 1937 in this country still accounted for 11% of deaths of infants under 2 years, or over 3,000 deaths. After removing diarrhœa due to poor hygiene and dirty milk, that which remains is due to two major, and several minor, causes; the two major being (1) specific infection with intestinal pathogenic organisms or protozoa, and (2) associated parenteral infection.

In 1925 Marriott pointed out the association of diarrhœa with infection elsewhere in the body, especially the upper respiratory tract, and therapy began to be directed towards eradicating this infection. However, no direct causal relationship could be proved although important information was derived from a study of the problem. It was noted that common infecting organisms were staphylococci and streptococci, both of which produce an enterotoxin; that infants had a smaller amount of acid in their stomachs than older children, secretion of which was inhibited by infection and which was neutralized by cow's milk; this lack of acid was thought to enable *B. coli* to multiply in the upper reaches of the intestine and it was found that filtrates from cultures of *B. coli* led to diarrhœa and vomiting when fed to animals.

The common association of parenteral infection with diarrhœa, even if not causative, leads to serious therapeutic problems which may be considered along the following lines:

Diagnosis.—Each baby must be considered as an individual problem and attempts should be made at the same time to prove or disprove the presence of either a specific intestinal infection or an associated parenteral infection. The finding of pathogenic organisms in respiratory tract or urine may be the only proof of the latter.

Isolation.—Although individual isolation is desirable for all babies in hospital the aims of isolation in patients with diarrhœa should be clearly defined. A baby with dysentery is isolated more for the safety of others because its stools are infective, while a baby with parenteral diarrhœa, if dangerous at all, is isolated because of possibly causing airborne upper respiratory infection.

Treatment.—The extent of this depends on the severity of the case. It must be remembered that, while a well-marked case of dehydration and acidosis is easy to recognize, it is easy to underestimate the degree of dehydration in a very fat child and overestimate it in a very thin child. Any baby with this condition may become desperately ill in a very few hours. In general, therapy has to be directed towards (1) supplying proper amounts of fluid, electrolytes and plasma proteins: in any severely ill patient this has to be done by parenteral routes which requires technical skill and

(trilene) analgesia has been discussed. A simple apparatus has been described by means of which the patient may administer to himself with safety a mixture of "trilene" vapour and air for the production of analgesia. Experiments made with this apparatus have been outlined and the clinical application of the analgesia in 62 cases has been reported upon.

The advantages of the method are: (1) Analgesia may be safely administered without medical supervision. (2) No attention is called for by the apparatus during administration. (3) The analgesia may be employed during operation in the mouth without risk of inhalation of foreign material into the lungs. (4) The apparatus is portable and independent of gas cylinders. (5) Economy (1 hour of analgesia costs 3d. approx.).

The disadvantages are: (1) The analgesia calls for muscular exertion on the part of the patient and would be inapplicable for long administrations. (2) A varying period (usually one and a half to two minutes) is required in which to induce analgesia. (3) The method requires a co-operative patient and is difficult to apply where heavy premedication has been given. (4) Certain cases (in the series quoted 12% approx.) appear to derive no benefit from the analgesia and it would appear that there is no way of ascertaining this fact in a patient before applying the analgesia.

REFERENCES
HARTRIDGE, H. (1920) in Starling's Principles of Human Physiology, 3rd Edition. London.
HEWER, C. LANGTON (1941) *Brit. med. J.* (i), 924.
—— (1942) *Proc. R. Soc. Med.*, **35**, 463.
MENNELL, Z (1933) *Practitioner*, **130**, 519.
WILSON, S R. (1927) *Proc. R. Soc. Med.*, **20**, 1301.

A film showing the application of self-administered analgesia with trilene in five cases was shown at the meeting.

Mr. Guy H. Ellingham gave an account of a series of over one hundred cases of self-induced trilene analgesia for dental purposes. He said that in every single case the induction and recovery had been uneventful and had not given the slightest cause for alarm, and from this he suggested that Dr. Hill's apparatus used for the dental patient could be considered as absolutely safe. Five per cent. of his cases he considered failures, these because of nervousness and lack of co-operation. Of the remaining 95%, the analgesia produced was quite adequate in the majority of cases, helpful in all. Many patients preferred it to the local anæsthesia of which they had experience, and asked for it again on other occasions. Mr. Ellingham thought that the contra-indications were: (1) Very nervous and unco-operative patients (although some such had been helped by trilene in a dramatic manner, and he did not think it possible to differentiate between those highly strung patients who would, or those who would not, be helped by it). (2) Precision cavity preparation, e.g. for inlays or other work which might take a considerable time.

He thought the use of trilene was strongly indicated: (1) When two or more cavities in different parts of the mouth had to be prepared at the same sitting. (2) For the opening of pulp canals in acute cases. (3) For the removal of loose and periostitic teeth where local anæsthesia was contra-indicated. (4) For the opening of abscesses and other minor surgical procedures. (5) For the treatment of painful gum conditions such as Vincent's disease. (6) Administered in addition to local anæsthetics for the tranquillizing and relaxing effect, e.g. operations on the third molar.

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*March* 24, 1944]

DISCUSSION ON PARENTERAL DIARRHŒA

Major T. F. McNair Scott, U.S.A.M.C.: The term parenteral diarrhœa connotes in the minds of pædiatricians diarrhœa associated with infection outside the alimentary tract. No definite pathology in the intestine itself can be found.

Diarrhœa has always been a major problem facing physicians in charge of children, particularly in the first two years of life. During the early part of the century it was a leading cause of death in infants under 2 years old, the main incidence occurring in the summer months. Investigation pointed to contaminated milk and poor hygiene as being the most important factors in this seasonal incidence and improvement in public health education and hygiene led to a decline of this summer diarrhœa. Although summer diarrhœa was of predominating importance, study of notifications reveals that a certain amount of diarrhœa occurred all through the year and that its incidence had not been lowered by the above measures. It was only when the incidence of summer diarrhœa fell below the level of this all-season diarrhœa, between 1920 and 1930, that the latter attracted attention. This residuum of diarrhœal diseases in 1937 in this country still accounted for 11% of deaths of infants under 2 years, or over 3,000 deaths. After removing diarrhœa due to poor hygiene and dirty milk, that which remains is due to two major, and several minor, causes; the two major being (1) specific infection with intestinal pathogenic organisms or protozoa, and (2) associated parenteral infection.

In 1925 Marriott pointed out the association of diarrhœa with infection elsewhere in the body, especially the upper respiratory tract, and therapy began to be directed towards eradicating this infection. However, no direct causal relationship could be proved although important information was derived from a study of the problem. It was noted that common infecting organisms were staphylococci and streptococci, both of which produce an enterotoxin; that infants had a smaller amount of acid in their stomachs than older children, secretion of which was inhibited by infection and which was neutralized by cow's milk; this lack of acid was thought to enable *B. coli* to multiply in the upper reaches of the intestine and it was found that filtrates from cultures of *B. coli* led to diarrhœa and vomiting when fed to animals.

The common association of parenteral infection with diarrhœa, even if not causative, leads to serious therapeutic problems which may be considered along the following lines:

Diagnosis.—Each baby must be considered as an individual problem and attempts should be made at the same time to prove or disprove the presence of either a specific intestinal infection or an associated parenteral infection. The finding of pathogenic organisms in respiratory tract or urine may be the only proof of the latter.

Isolation.—Although individual isolation is desirable for all babies in hospital the aims of isolation in patients with diarrhœa should be clearly defined. A baby with dysentery is isolated more for the safety of others because its stools are infective, while a baby with parenteral diarrhœa, if dangerous at all, is isolated because of possibly causing airborne upper respiratory infection.

Treatment.—The extent of this depends on the severity of the case. It must be remembered that, while a well-marked case of dehydration and acidosis is easy to recognize, it is easy to underestimate the degree of dehydration in a very fat child and overestimate it in a very thin child. Any baby with this condition may become desperately ill in a very few hours. In general, therapy has to be directed towards (1) supplying proper amounts of fluid, electrolytes and plasma proteins: in any severely ill patient this has to be done by parenteral routes which requires technical skill and

skilled nursing; (2) treatment of infection by the proper use of sulphonamides and surgical interference where called for; (3) dietary regulation in which a period of starvation is followed by a slowly incremented diet up to basic caloric needs, at which level it is maintained until tolerance is regained. It is important to treat the patient and not the stools and to remember that severe malnutrition may supervene upon the diarrhœa. Vitamins should be supplied, if necessary, parenterally. The majority of babies treated along these lines get well but a certain percentage do not. It is in this group that new therapeutic procedures are apt to be tried; while in any given individual such a new procedure, e.g. mastoidectomy, may be life-saving, it is important not to stress this procedure at the expense of the basic essential treatment outlined above.

Dr. William Gunn (London County Council) described parenteral diarrhœa, which appeared under many guises and names, as the most baffling as it was the most prevalent and fatal of diseases in young children, especially in infants under 1 year: perhaps in its typical form it only occurred at that age, for there did not appear to be any good reason to regard neo-natal diarrhœa, i.e. occurring in the first 28 days of life, as a different disease although some authorities held that view. He showed diagrams of the incidence and time-relations of coryza, pharyngitis and tonsillitis (24 cases), bronchitis and pneumonia (76 cases), suppurative otitis media (17 cases), compared with enteritis (80 cases comprising 6·8% of the total admissions) amongst the inmates of a residential London nursery of 50 beds, through which a total of 1,170 children passed in 1943 to reception areas, the average duration of stay being just over sixteen days. No close correlation was evident between these infections except for a short period in the middle of the year, but due allowance must be made for the intervals which usually separate the onset of the parenteral infection and the resultant diarrhœa, which succeeds it in one to seven days, and is itself succeeded by otitis media after a variable interval, sometimes amounting to some weeks. Just over one-third of the 80 cases were admitted to the North-Western Fever Hospital for treatment and 24 were diagnosed as acute gastro-enteritis; evidence of parenteral infection was found in 19, viz. coryza 6, otitis media 6, mastoiditis 3, bronchitis 2, pneumonia 2 (1 tuberculous). The 3 cases in which the diagnosis was not confirmed were due to: measles, Sonne dysentery, intestinal giardiasis, 1 each. Tables were shown detailing the yearly admissions and case-fatality rates for acute gastro-enteritis at the North-Western Hospital for the eight years 1936 to 1943, by quarters and specific age-groups. Both prevalence and fatality were fairly evenly distributed over the whole year with the highest incidence in the last two quarters and highest fatality in the first two for the whole period, but there were considerable fluctuations in the different years. Attack and fatality rates were highest in the three to six months group, but again this did not hold for every year.

A representative sample of 89 consecutive cases was analysed in detail: 13 were subjected to bilateral mastoidectomy; suppuration was found in 12. Sulphonamides, chiefly sulphapyridine and sulphamezathine, were given to a majority and sulphaguanidine or sulphasuxidine to a minority without clear-cut results. Dr. Gunn urged that every patient should be nursed in a separate room with facilities for an "aseptic" nursing technique, as good nursing care was perhaps more important in lowering fatality than strictly medical or surgical measures by themselves.

Dr. Patria Gairdner (Oxford C.C.): It has long been recognized that infantile diarrhœa is a disease which shows "a preponderance among artificially fed infants of urban poor-class districts" (*Lancet*, 1943 (ii), 769). The enormous reduction in the incidence of "summer diarrhœa" that has occurred since 1911 is also a familiar fact, with the consequent levelling of the incidence throughout the year.

The following tables, derived from the figures given in the Registrar-General's Statistical Reviews for England and Wales, confirm the high incidence of this disease among urban as compared with rural infants. Less familiar is the distressingly high incidence in Greater London, even in the Outer Ring, an area which, consisting as it does of residential suburbs, is characterized by a remarkably low mortality from the other diseases of infancy.

TABLE I.—INFANT MORTALITY FROM ALL CAUSES AND FROM DIARRHŒAL AND NON-DIARRHŒAL DISEASES, ACCORDING TO DEGREE OF URBANIZATION—1935-38.

	Infant mortality	Diarrhœal mortality	Non-diarrhœal mortality
England and Wales	56·4	5·6	50·6
Greater London	52·8	8·6	44·2
London (Admin. Co.)	60·3	12·1	48·2
Greater London (Outer Ring)	46·5	5·7	40·3
County Boroughs	63·3	5·9	57·4
Urban Districts	53·8	3·3	50·5
Rural Districts	49·6	2·4	47·2

The high diarrhœal death-rate in London is outstanding, particularly in the Administrative County, but even the outer ring, with its non-diarrhœal mortality by far the lowest in the above table, has a higher death-rate from this one disease than obtains in the country as a whole.

GEOGRAPHICAL DISTRIBUTION

Excluding Greater London, the geographical regions having the highest infant mortality (North I and North IV) have the highest mortality from infantile diarrhœa. This may be shown by plotting the diarrhœal mortality for the years 1931-38 against the non-diarrhœal mortality over the same period in the eleven geographical regions into which the Registrar-General divides England and Wales outside Greater London. The two values are highly correlated (r = + ·80 ± ·31). When, however, Greater London is included in the calculation, with its high diarrhœal and low non-diarrhœal death-rates, the co-efficient of correlation falls to the insignificant value of + ·30 ± ·3.

GEOGRAPHICAL DISTRIBUTION AND AGE INCIDENCE

The heavy incidence of infantile diarrhœa in Greater London is not equally distributed over the first twelve months of life. Whereas the areas of high total infant mortality (e.g. North I and North IV) show a comparatively high diarrhœal death-rate in the early weeks of life, the corresponding rate in London is below that for the country as a whole. It is during the succeeding months that the London rate rises steeply—in fact, during these months diarrhœa is the chief cause of infants' deaths in this area.

In the following tables the diarrhœal and non-diarrhœal mortalities are shown, and the ratio of one to the other, for England and Wales, Greater London, and two areas of high and two of low infant mortality.

TABLE II.—DIARRHŒAL (D.M.) AND NON-DIARRHŒAL MORTALITY (N.D.M.) BY AGE IN GEOGRAPHICAL REGIONS—1931-38.

			Under 1 month		1 to 3 months		3 to 12 months	
			D.M.	N.D.M.	D.M.	N.D.M.	D.M.	N.D.M.
England and Wales	...	...	0·52	30·66	1·42	7·14	3·36	16.36
Greater London	...	...	0·42	24·33	1·96	7·50	5·80	15·17
North I	...	...	1·13	36·58	1·89	10·04	4·51	21·74
North IV	...	...	0·61	33·94	1·67	9·96	3·53	21·49
East	...	...	0·26	28·56	0·59	6·75	1·32	12·22
South-West	...	...	0·37	23·40	0·66	6·76	1·09	11·03

TABLE III.—PERCENTAGE DIARRHŒAL OF NON-DIARRHŒAL MORTALITY BY AGE AND GEOGRAPHICAL REGION—1931-38.

				Under 1 month	1 to 3 months	3 to 12 months
England and Wales	...	...	...	1·7	19·3	20·5
Greater London	...	...	...	1·7	26·1	38·3
North I	...	...	...	3·1	18·3	20·7
North IV	...	...	...	1·8	16·8	20·7
East	...	...	...	0·91	8·7	10·8
South-West	...	...	...	1·3	9·8	9·9

When London is compared with other large cities, only Newcastle, with its extremely high total mortality, has a higher death-rate from infantile diarrhœa. In the following table four cities are included, each of which is the centre of a large, more or less completely urbanized area, and is thereby more comparable with London than is the aggregate of County Boroughs. It may be observed that, even where the diarrhœal mortality is high, the ratio of diarrhœal to non-diarrhœal death-rates is considerably lower than that found in the administrative County of London.

TABLE IV.—INFANT MORTALITY. (1) FROM ALL CAUSES (I.M.); (2) DIARRHŒA (D.M.); (3) OTHER CAUSES (N.D.M.) AND PERCENTAGE (2) OF (3).

London and Certain County Boroughs 1935-38.

			(1) I.M.	(2) D.M.	(3) N.D.M.	% (2) of (3)
London (Admin. Co.)	...	...	60·3	12·1	48·2	25·1
Greater London	...	...	52·8	8·6	44·2	19·5
Outer Ring	...	...	46·5	5·7	40·8	14
Birmingham	...	...	62·2	6·9	55·3	12·5
Manchester	...	...	74·2	5·8	68·4	8·5
Newcastle	...	...	83	13·8	69·2	19·9

LEGITIMACY

Infantile diarrhœa is second only to congenital syphilis in its high illegitimate: legitimate ratio. The ratio of the two death-rates is also markedly higher in London than it is elsewhere.

TABLE V.—RATIO OF DEATH-RATES AMONG ILLEGITIMATE TO THOSE AMONG LEGITIMATE INFANTS—1935-38

	All causes	Diarrhœa
England and Wales	1·57	2·33
Greater London	2·14	3·26
County Boroughs	1·40	1·72
Urban Districts	1·43	1·74
Rural Districts	1·49	1·97

The diarrhœal death-rates among London's illegitimate infants is so high that such an infant has a one in forty chance of dying of this disease before reaching its first birthday.

CONCLUSION

It is difficult to see what environmental factor is at work which so favours the spread of this disease in London and its suburbs, where other causes of infant death are not ill-controlled. Environmental factors are usually found to affect especially the mortality during the later months of infancy, and it is during these months that London's diarrhœal death-rate so far exceeds that found elsewhere.

The graph (not reproduced) shows that, until 1929, the rates for London and for the aggregate of county boroughs follow one another closely, sometimes one, sometimes the other being the higher. For the last ten years for which figures are available, however, it will be seen that the county borough rate has fallen on the whole, whereas that for London was tending to rise during the pre-war years. Judging by recent clinical experience there does not seem to have been a reversal of this trend during the past five years.

No explanation is offered to account for this curious distribution of diarrhœal mortality. It is to be hoped that further studies will bring to light the factors at work in London which prevent its sharing in the nation-wide fall in the death-rate from infantile diarrhœa.

I wish to express my gratitude to Dr. W. T. Russell for his generous help in the preparation of the tables.

Dr. C. H. Andrewes (Nat. Instit. for Med. Research): Three explanations of "Parenteral Diarrhœa" seem possible: (i) Dr. Cruickshank thinks the concurrence of respiratory lesions and diarrhœa may be merely coincidental; the figures presented to-day make that rather hard to believe. (ii) The diarrhœa may be due to a reaction to respiratory infection on the part of children with a particular constitution. (iii) There may be a specific infection of the respiratory tract with a tendency both to cause diarrhœa and to facilitate bacterial secondary infections, e.g. of the middle ear. I should have thought that available data as to incidence should allow us to distinguish between (ii) and (iii). (iii) would be indicated if the incidence of " parenteral diarrhœa " showed a sufficiently wide divergence from that of respiratory infections generally.

Is the term "parenteral diarrhœa" so firmly established that it cannot be altered? The juxtaposition of those two words seems to the uninitiated quite absurd, and few appreciate without explanation what is the idea underlying the term.

Dr. M. Mitman (London County Council): It is very satisfactory to hear that epidemiologists regard the problem of infantile diarrhœa, whether of enteral or parenteral origin, as one of infection. In the absence of definite knowledge of the causal agent and the mode of spread I think individual isolation important in the treatment of cases. Its success in preventing diarrhœa has been proved by the use of the Dick Diet-Kitchen and Aseptic Nursing Technique in the Cradle of Evanston (Sauer, 1935). In my experience parenteral infections are found in about 30% of cases and proof is lacking that they are causal.

Reference.—SAUER, L. W. (1935), *J. Pediat.*, 6, 753.

Dr. A. H. Gale (Board of Education): An interesting feature of the long term mortality of infantile diarrhœa is the comparatively sudden fall after 1911. In 1911 the rate in England and Wales was 36 per 1,000 births out of a total infantile mortality rate of 130. Subsequently the rate never rose above 20 and after 1915 rose above 11 only on one occasion (1921—14).

[*April* 28, 1944]

DISCUSSION ON THE ORGANIZATION AND ADMINISTRATION OF EPIDEMIOLOGICAL INQUIRIES

Dr. R. N. Curnow (Cornwall C.C.): The fundamental points in an epidemiological inquiry are: ascertainment of the existence of an outbreak; administrative responsibility for organizing the inquiry; the epidemiological team; and then possible improvements in the present service.

Ascertainment of an outbreak.—The Medical Officer of Health is usually made aware of an outbreak by notification through the usual channels. Formal notification is sometimes, slow and incomplete; liaison with the bacteriologist and the fever hospital will often give information long before formal notification. Nevertheless formal notification is an indispensable indicator for which there is, no substitute. Dysenteric infections, mild pemphigus, the so-called reactionary temperatures in a maternity ward, and other infections of a similar character sometimes quietly run their course for a long time before the need for an investigation becomes apparent. Once the importance of the epidemiological outlook is appreciated, sequences of events become suggestive; for example, in a residential nursery containing some 35 infants, four infants died in less than two years, the causes of death being, considered to be meningococcal septicæmia; tuberculous meningitis (after an illness of a few days); influenza (there were no other cases at the time) and pneumonia respectively. Post-mortem examination corrected the diagnosis in the last case to meningococcal septicæmia. The only nurse present on the staff throughout the whole period was a carrier of *N. meningitidis* Group 1 at the time of the first case, then became negative; then persistently positive on examination after the last case. She has been transferred from the nursery; the sequence of events in this nursery is suggestive though not conclusive, but strongly indicates the importance of developing the epidemiological point of view.

The cause of this delay in appreciating the epidemiological nature of certain illnessses is undoubtedly due to some deficiency in our medical education coupled with the difficulty under present arrangements of diffusing to the medical profession as a whole the recent rapid advances in bacteriology and epidemiology. Reforms in the teaching of epidemiology have already been suggested by the Social and Preventive Medicine Committee of the Royal College of Physicians of London.

The administrative responsibility for organizing an epidemiological inquiry should rest definitely on one individual otherwise delay and indecision will hamper the investigation. This is difficult in a county area.

The medical officer of health is responsible for organizing an investigation into an outbreak of infectious disease. In a county borough there is no ambiguity about such a statement because there is only one medical officer of health of a county borough; in a county, however, there are two medical officers of health concerned in each part of the county, namely, the medical officer of health of the county district and the medical officer of health of the county. The powers and duties relating to the prevention and treatment of notifiable diseases are placed upon the councils of the county districts and not upon the County Councils; the Sanitary Officers (outside London) Regulations 1935, place upon the medical officer of health of a county district the duty of informing himself as far as is practicable respecting all matters affecting or likely to affect public health in the district and of being prepared to advise the local authority on any such matter. The Public Health (Infectious Diseases) Regulations 1927 place the duty of investigating outbreaks of certain infectious diseases clearly upon the medical officer of health of the county district. Notifiable diseases are notified by the medical practitioner to the medical officer of health of the district concerned so therefore it seems clear that the primary responsibility for organizing an inquiry into an outbreak of infectious disease in a county rests upon the medical officer of health of the district council, but further consideration will show that the county medical officer is intimately concerned.

He also, under the Sanitary Officers (outside London) Regulations 1935, is charged with the duty of informing himself as far as practicable respecting all matters affecting or likely to affect the public health in the county and of being prepared to advise the County Council on any such matter. As school medical officer he is concerned jointly with the medical officer of health of the county district with arrangements to prevent the spread of infection in the schools administered by the County Council as the local education authority. The intricate relationship and division of duties between the local sanitary authority and the education authority in connexion with the control of infection in schools has been the subject of a memorandum on the Closure of and Exclusion from Schools issued jointly by the Ministry of Health and the Board of Education.

LEGITIMACY

Infantile diarrhœa is second only to congenital syphilis in its high illegitimate: legitimate ratio. The ratio of the two death-rates is also markedly higher in London than it is elsewhere.

TABLE V.—RATIO OF DEATH-RATES AMONG ILLEGITIMATE TO THOSE AMONG LEGITIMATE INFANTS—1935-38

				All causes	Diarrhœa
England and Wales	...	...	...	1·57	2·33
Greater London	...	...	...	2·14	3·26
County Boroughs	...	...	...	1·40	1·72
Urban Districts ...	...	...	...	1·43	1·74
Rural Districts ...	...	...	...	1·49	1·97

The diarrhœal death-rates among London's illegitimate infants is so high that such an infant has a one in forty chance of dying of this disease before reaching its first birthday.

CONCLUSION

It is difficult to see what environmental factor is at work which so favours the spread of this disease in London and its suburbs, where other causes of infant death are not ill-controlled. Environmental factors are usually found to affect especially the mortality during the later months of infancy, and it is during these months that London's diarrhœal death-rate so far exceeds that found elsewhere.

The graph (not reproduced) shows that, until 1929, the rates for London and for the aggregate of county boroughs follow one another closely, sometimes one, sometimes the other being the higher. For the last ten years for which figures are available, however, it will be seen that the county borough rate has fallen on the whole, whereas that for London was tending to rise during the pre-war years. Judging by recent clinical experience there does not seem to have been a reversal of this trend during the past five years.

No explanation is offered to account for this curious distribution of diarrhœal mortality. It is to be hoped that further studies will bring to light the factors at work in London which prevent its sharing in the nation-wide fall in the death-rate from infantile diarrhœa.

I wish to express my gratitude to Dr. W. T. Russell for his generous help in the preparation of the tables.

Dr. C. H. Andrewes (Nat. Instit. for Med. Research): Three explanations of "Parenteral Diarrhœa" seem possible: (i) Dr. Cruickshank thinks the concurrence of respiratory lesions and diarrhœa may be merely coincidental; the figures presented to-day make that rather hard to believe. (ii) The diarrhœa may be due to a reaction to respiratory infection on the part of children with a particular constitution. (iii) There may be a specific infection of the respiratory tract with a tendency both to cause diarrhœa and to facilitate bacterial secondary infections, e.g. of the middle ear. I should have thought that available data as to incidence should allow us to distinguish between (ii) and (iii). (iii) would be indicated if the incidence of "parenteral diarrhœa" showed a sufficiently wide divergence from that of respiratory infections generally.

Is the term "parenteral diarrhœa" so firmly established that it cannot be altered? The juxtaposition of those two words seems to the uninitiated quite absurd, and few appreciate without explanation what is the idea underlying the term.

Dr. M. Mitman (London County Council): It is very satisfactory to hear that epidemiologists regard the problem of infantile diarrhœa, whether of enteral or parenteral origin, as one of infection. In the absence of definite knowledge of the causal agent and the mode of spread I think individual isolation important in the treatment of cases. Its success in preventing diarrhœa has been proved by the use of the Dick Diet-Kitchen and Aseptic Nursing Technique in the Cradle of Evanston (Sauer, 1935). In my experience parenteral infections are found in about 30% only of cases and proof is lacking that they are causal.

Reference.—SAUER, L. W. (1935), *J. Pediat.*, 6, 753.

Dr. A. H. Gale (Board of Education): An interesting feature of the long term mortality of infantile diarrhœa is the comparatively sudden fall after 1911. In 1911 the rate in England and Wales was 36 per 1,000 births out of a total infantile mortality rate of 130. Subsequently the rate never rose above 20 and after 1915 rose above 11 only on one occasion (1921—14).

of epidemiologists either with field staffs of assistant medical officers, health visitors and sanitary inspectors, or with the right at any moment to commandeer the staff of medical officers of health who would no longer themselves be responsible for epidemiological inquiries; the first method of staffing would be extravagant, the second impossible.

Much of the present public health administration is occupied with arrangements designed to prevent the outbreak of infectious disease, so that the severance of the epidemiological from the general public health services would produce a curious situation in which one service was concerned with the prevention of infections and another with the suppression of declared infection. This dichotomy would inevitably retard the speed of ascertainment of infection. Information on all health matters naturally flows into the health office and a duplication of the channels of communication must be confusing; for instance, is the midwife to notify the health office that she has had to summon medical aid, and a different office that she has been in contact with infection? Is her general work to be inspected by one supervisor and her disinfection by another? In the series of deaths in a nursery which I have already described, the situation was revealed in connexion with general health administration and not as part of a formal epidemiological service.

Moreover, the administration of an epidemiological inquiry requires not only a knowledge of bacteriology or of the epidemiology of individual diseases, it requires also a familiarity with local government procedure, with the powers and duties imposed by legislation, and experience in public health administration. So many new epidemiologists with the requisite knowledge and experience could only be derived from one source—the present public health services—there is no alternative, and thus we should find ourselves back more or less at the starting point except that we should have made the present situation still worse confounded. Further consideration would only serve to make still more evident the obvious conclusion that epidemiology and the other branches of the health services are so interwoven as to be inseparable and there has been no such failure of the present services as would justify artificial experimentation with a new service with such obvious defects. On the contrary, the present services are generally so satisfactory that all that is needed is a welding together and strengthening of the present epidemiological service within the public health service itself.

In a public health epidemiological service, the staff of the health department—assistant medical officers, health visitors, sanitary inspectors, and clerks—can be transferred from one public health duty to another as the need arises, in epidemic time to form part of an epidemiological team and in quiet times to carry on with their normal public health duties, but having instruction in epidemiological methods from time to time from the medical officer who specializes in epidemiology. Such a medical officer with his training in public health and experience in the administration of a health department finds it easy to organize and operate a public health team in field work which has for a very long time been one of the normal functions of a health department, and which in the health services of the future will surely contribute still more to a system of general medical research. If he were recognized as of specialist status he could do more than could any legislative reform to secure early ascertainment of epidemic disease by interesting members of the profession in this fascinating subject at meetings of medical societies and other informal gatherings.

In county boroughs there has been no difficulty in arranging such a service. In county areas the administrative muddle makes it more difficult. It is a matter of the first importance to produce a uniform comprehensive service in counties as well as in county boroughs. There are two alternatives—either to concentrate the service on the minor authorities or on the County Councils. The general tendency is towards placing the responsibility for these larger services more upon the shoulders of the major authorities. The proposals in the Education Bill are that County and County Borough Councils will be the authorities primarily responsible for the education services, with arrangements for delegation to some of the existing authorities; it is suggested that the Maternity and Child Welfare Clinic Services shall follow the Education Services. The Midwifery Services in counties will probably remain with the County Councils. There is a general movement towards basing the Specialist Medical Services on larger areas, for it is clear that skill in any specialty depends on a wide and continuous experience as well as on training and qualifications. In the small area outbreaks of infection occur at irregular intervals, at one time being heavy and almost overwhelming but with long quiet periods during which it is difficult to maintain interest and which interrupt that steady flow of experience so necessary to efficiency. Problems caused by outbreaks of the less common infectious diseases cause acute anxiety when they are encountered at long intervals, but can be tackled more thoroughly as a matter of general routine in a service which covers a wide area. Our own experience in providing a County Council Isolation Hospital for the greater part of the County of Cornwall has shown that the

Under the maternity and child welfare arrangements, the county medical officer is also directly responsible for dealing with infectious cases. In those parts of the county where the County Council is the local supervising authority under the Midwives Acts, a midwife who considers herself likely to be a source of infection, notifies the county medical officer direct and it is his duty to suspend her from practice if necessary.

Although notifications by medical practitioners almost invariably go to the medical officer of health of the district council who makes a weekly return to the county medical officer there is an exception—ophthalmia neonatorum—where the notification is sent by the medical practitioner direct to the medical officer of health of the maternity and child welfare authority which in county areas includes the County Council to a greater or lesser extent.

Some district councils are the elementary education authorities with their own school medical service and some are not; some district councils are maternity and child welfare authorities, responsible for their own maternity and child welfare arrangements and some are not; some are local supervising authorities under the Midwives Acts and some are not; I have known of a borough which was a maternity and child welfare authority only; several which also provide a school medical service but not a midwifery service and a number which provide all these; of course many local authorities provide none of these services; the County Council is responsible so far as these services are concerned for areas of the county of varying size for each service not already provided by the minor authorities; so that the duty of investigating an outbreak of infectious disease in a school or in connexion with midwifery practice varies in a county from one part to another, in some places being the responsibility of the county medical officer either as such or as the school medical officer, and in other places being the responsibility of the medical officer of health of the district council. In addition, both are charged with the duty of informing themselves as far as practicable respecting all matters affecting or likely to affect the public health of their areas.

Under present circumstances the only solution to the problem lies in the establishment of a satisfactory *modus vivendi* between the county medical officer and the medical officers of health of district councils, but even so, the complications unnecessarily created by the present administrative structure should clearly be resolved at the earliest possible moment.

The outbreak having revealed itself and the responsibility for organizing an inquiry having been settled, the next step is to bring into operation *the epidemiological team*. An investigation into an outbreak of infectious disease is one of the most outstanding examples of the success of medical team-work. The team will consist of the medical officer of health, the bacteriologist, the medical superintendent of the Isolation Hospital, and the medical statistician, with a field survey staff of assistant medical officers, health visitors, and sanitary inspectors as required. The investigation is planned at the outset by a conference at which the bacteriologist explains the help he can afford and the precision which bacteriology has reached in the particular disease under review. In these matters he is able to keep pace with the growth of knowledge through the excellent Emergency Public Health Laboratory Service. Medical officers of health are utilizing the services of the Emergency Public Health Laboratory Service whose bacteriologists have willingly undertaken field inquiries with conspicuous success. It is impossible to over-estimate the help of a statistician in certain types of inquiry. There is a mass of published evidence on the value of the statistical approach, and most of us have had some experience of its value. For instance, in an investigation into an outbreak of vomiting in Cornish schools undertaken in Cornwall by Dr. E. C. H. Huddy, a survey on purely statistical lines indicated quite clearly that the vehicle of infection was the school milk supply while the school canteen was completely exonerated. The medical superintendent of the Isolation Hospital who may well be the first to know of an epidemic confirms or corrects the clinical diagnosis of the cases, and his co-operation with the bacteriologist is a vital factor in the success of the inquiry. The medical officer of health is responsible for the general organization of the survey which is often undertaken by a member of the staff of the health department who has taken a special interest in epidemiology. Such an epidemiologist tries to keep up to date by reading the literature, including the very informative monthly bulletins issued by the Ministry of Health and the E.P.H.L. Service, but the arrangements for post-graduate study and regular discussions are inadequate. Beyond this team there is always the opportunity in difficult inquiries of obtaining advice and help from one of the expert epidemiologists of the Ministry of Health.

For a *future policy* the creation of a completely new epidemiological service separate from the other public health services may be urged on the grounds of the rapid advance in bacteriology. It would involve the setting up of a complete new staff of large numbers

the laboratory diagnosis of established infections more reliable, but they have rendered more easy the detection of pathogenic bacteria in convalescents and in healthy contacts and in materials outside the human body—for example, streptococci and diphtheria bacilli in dust or milk and enteric organisms in sewage and water.

The part played by the infected healthy contact (subclinical infection) in the spread of disease has, of course, been recognized for years, even before the work of Dudley established the importance of this factor in diphtheria. Reports in the Monthly Bulletin of the Emergency Public Health Laboratory Service provide numerous instances of such subclinical infections in relation to outbreaks of scarlet fever and other streptococcal infections, diphtheria, dysentery and Salmonella infections. In the outbreak of water-borne paratyphoid at Brixworth reported in the Monthly Bulletin of February 1942, there were four typical clinical cases, but 21 of 30 other persons at risk excreted para-typhoid bacilli in the fæces and of these many showed no clinical evidence of their infection; the examination of contacts in a recent paratyphoid outbreak in Dundee disclosed a number of apparently healthy persons who were harbouring one or other of six different types of Salmonella organisms (Davidson and Brodie, 1944). In outbreaks of undulant fever due to *Brucella abortus*, examination of the serum of those consuming the infected milk has shown that subclinical infections may greatly outnumber the clinical cases (Elkington *et al.* 1940; Cruickshank, J. C., and Stevenson, 1942). The detection of these subclinical infections and convalescent carriers is usually possible only by laboratory tests and work in the last few years has shown that in many outbreaks of infectious disease such infections are more widespread than many of us suspected.

The improved methods of isolating pathogenic bacteria from dust and air have yielded results which have considerably modified our ideas on the mode of spread of upper respiratory tract infections (Cruickshank, R., 1942).

(2) The recognition by cultural or serological methods of types within pathogenic species of bacteria has made considerable progress and the application of these methods has been of particular value in epidemiological work.

(*a*) In this country there seems to have been little occasion to utilize serological typing in the investigation of outbreaks of pneumococcal infection, but in America the work of Smillie and others has shown how pneumococcal typing has enabled the spread of an epidemic type of pneumococcus in a community to be followed (Gilman and Anderson, 1938; Smillie and Jewett, 1940).

(*b*) The value of serological grouping and typing of hæmolytic streptococci has been established by numerous reports during the last few years. It has been possible to trace the spread of a particular strain among staff and patients in a hospital ward, even though only a proportion of those infected developed symptoms. In general it is doubtful whether the work involved in detecting the carriers of an epidemic strain of hæmolytic streptococci in a community such as a school or nursery is justified by the result obtained by measures based on the findings. The repeated swabbing of pupils and staff in a school and the serological identification of the hæmolytic streptococci isolated may be quite a formidable task. Whether the work is to be undertaken or not will depend not only on the laboratory facilities available but on such factors as the extent of declared infection, the stage of the outbreak and the nature and size of the population at risk. When inquiring into cases of streptococcal puerperal sepsis, one cannot incriminate the midwife simply on the finding of hæmolytic streptococci in her throat. It may be advisable to suspend her from duty if the streptococci isolated from her prove to belong to Group A; but before she can be considered on the bacteriological evidence as the likely source of infection, it is necessary to show that the streptococcus carried by the midwife is serologically identical with that infecting the patient.

(*c*) The typing of diphtheria bacilli may also be of value in tracing sources of infection. In 1940 and 1941 one or other of the three types tended to be prevalent in different localities of the Eastern Region. When, as occasionally happened, a case occurred due to a type not previously encountered in a particular district, inquiry usually discovered, in close proximity to the case, a recently evacuated child who was carrying the new type.

(*d*) It is perhaps the bacteriophage typing of the enteric bacteria that has made possible the most spectacular results in recent epidemiological work. In 1938 Craigie (Craigie and Yen, 1938*a*) demonstrated that typhoid bacilli, all strains of which had previously been regarded as identical, could be subdivided into a number of types by his special bacteriophage technique. He showed (1938*b*) that these types were stable and that the discovery had great practical value in the investigation of typhoid outbreaks. In this country the work has been followed up by Felix (1943) who has extended the technique to *Bacterium paratyphosum* B (Felix and Callow, 1943). The value of the method in field investigations has been well illustrated by Bradley's account of the

centralization of the treatment of infectious disease produces a steadier flow of cases, avoids the wild fluctuation which commonly takes place in smaller areas, and provides a wide experience in the diagnosis and treatment of different infections; so also with epidemiology. Moreover, epidemic disease is no respecter of local government boundaries. The numerous instances of epidemic disease contracted in the area of one minor authority developing in another and complicating investigation suggest that within reasonable limits the wider administrative area would prove more efficient.

In view of all these considerations it seems only reasonable that a specialist epidemiological service should become the responsibility of the major authorities.

It is therefore not surprising to read in the White Paper on "A National Health Service": "There will remain a field of day-to-day epidemiological work—many of the measures dealing with the notifications of the diseases, the local control of the spread of infection, and environmental factors affecting this, which are the subject of statutory powers under the Public Health Acts already—which can still be suitably carried out locally in the different parts of the joint authority's area, although it will probably be found that most of these activities should in future be centred in the County and County Borough Councils rather than distributed more widely, as they are now, over the districts of the minor authorities." Such an arrangement would in fact bring County Councils in line with County Borough Councils.

It is possible to envisage a uniform comprehensive epidemiological service in a county, flowing from the specialist epidemiologist on the headquarters staff down through the assistant medical officers who would hold "all-purpose" appointments as is already the case in many counties and who, under the guidance of the epidemiologist, could carry out the day-to-day routine epidemiological measures as part of their general duties.

So much for the local administration. There still remains the need for a more comprehensive organization which will weld together the epidemiological services of all the local authorities and ensure their continuing efficiency by stimulating interest, providing frequent discussions and descriptions of investigations, a centre staffed by men with the widest possible experience in epidemiology, available for consultation and assistance in case of serious local difficulties, and in this regard a continuation of the excellent consulting Epidemiological Services provided by the Ministry of Health. The Emergency Public Health Laboratory Service has greatly extended and organized the Bacteriological Services of the country. At the national centre there would be collected all the epidemiological experience gained in the field by the epidemiologists of the local authorities who would be given the opportunity of regular general meetings with bacteriologists and with statisticians to share their experiences and the various devices which each had found of value in his own area.

In such a way a simple but comprehensive Epidemiological Service could be provided for every part of the country—a central organization, both educational and consultative, passing down through a uniform Epidemiological Service provided by the major local authorities as part of their Health Services, and resting upon a well-informed profession keenly interested in the detection of epidemiological problems.

Prof. A. W. Downie (Liverpool): Before considering the laboratory side of epidemiological work there are two points which we should perhaps not overlook—the first is that much valuable work in tracing the source of outbreaks and devising methods for their control was done in the days before medical bacteriology had developed and the second point is that there is still a large number of epidemic diseases in which the bacteriologist can as yet give little help. How much can be achieved without such help has been demonstrated by Pickles of Aysgarth (1939). Nevertheless no one will quarrel with the statement that in certain infectious diseases, the application of modern bacteriological methods has furnished exact data which have materially increased our knowledge of the mode of spread of these infections and pointed the way to improved methods of control.

Recent Advances in Bacteriology of Special Value in Epidemiological Inquiry

During the last ten or fifteen years the advances in bacteriology which are of particular interest in relation to our subject may be considered under two headings: (1) Improvement in methods for the detection and isolation of pathogenic bacteria, and (2) improvements in methods for identifying bacterial types within a species.

(1) In the first category one may instance the use of gentian violet in blood agar plates for the isolation of *Streptococcus pyogenes*, the addition of penicillin to cough plates for the detection of *Hæmophilus pertussis*, the tellurite media for the diagnosis of diphtheria and the improved selective media for the detection of organisms of the typhoid, Salmonella and dysentery groups. Such improved methods have not only made

findings; but to avoid overlap and delay in setting in motion the machinery involved in the wider investigation which may be necessary, closer co-operation between the hospital pathologist, the medical officer of health and the local public health laboratory is desirable. Dr. Curnow has stressed the importance of stimulating the interest of the medical practitioner in epidemiological problems; this implies also a need to increase the appreciation of the medical profession generally of the help which the laboratory has to offer.

The outlying public health laboratories should be grouped around larger regional laboratories as exist to some extent in the Emergency Public Health Laboratory Service at present. These regional laboratories would serve as reference laboratories and might be associated with University departments of Bacteriology as in the north of England now. In addition to the specialist examinations which such laboratories could undertake, members of the staff should be given opportunities for carrying on intensive research in problems related to public health work. To these laboratories also, bacteriologists from subsidiary laboratories might be seconded from time to time to gain experience in special techniques or engage in research. Finally there would be need for a Central Institute having close association with the national epidemiological centre mentioned by Dr. Curnow. The central laboratory or institute would serve as a co-ordinating centre for the service where meetings might be held and courses of instruction given. It should also serve as a research centre where the problems of infection and immunity and methods of general and specific prophylaxis could be studied. Research in such problems has in the past, and will be in the future, vigorously pursued independently in medical schools and other laboratories or institutions, but there is room for a central institute for the Public Health Laboratory Service devoted to the study of epidemic disease.

Proper liaison between the public health laboratory and the medical officer is essential. The present system of sending duplicates of reports on laboratory findings to the local medical officer of health, the regional medical officer of the Ministry of Health as well as returns to the headquarters of the Emergency Public Health Laboratory Service, makes available, both locally and centrally, the information from the laboratory which may indicate the occurrence of infectious .disease requiring wider investigation. In the Eastern region frequent informal meetings between the staff of the Emergency Public Health Laboratory in Cambridge and medical officers of health are arranged at the Regional Office of the Ministry of Health. Personal contacts of this sort can be of the greatest value in promoting co-operation in epidemiological work.

The members of the Emergency Public Health Laboratory Service. under present conditions, engage to some extent in field inquiries: when a wider epidemiological service, such as Dr. Curnow visualizes, has been developed the bacteriologists may not be required to undertake so much field work. Nevertheless to obtain the greatest help from the laboratory, the epidemiologist should keep the bacteriologist constantly informed of the progress of an inquiry; the bacteriologist should have some training and experience in epidemiological work so that he may, when necessary, carry out field investigations. By so doing not only will the bacteriologist widen the interest of his own work, but his increased appreciation of the problems of the medical officer responsible for carrying out an inquiry will lead to better team-work. By such close association the epidemiologist may keep himself informed of advances in bacteriological methods and have a full appreciation of the help which the laboratory can bring to his problems.

REFERENCES

BRADLEY, W. H. (1943) *Brit. med. J.* (i), 433.
CRAIGIE, J., and YEN, C. H. (1938a) *Canad. publ. H th. J.*, 29, 448.
—— (1938b) *Canad. publ. Hlth. J.*, 29, 484.
CRUICKSHANK, J. C., and STEVENSON, G. A. (1942) *Brit. med. J.* (i), 522.
CRUICKSHANK, R. (1942) Control of Common Fevers, London, pp. 6 to 10.
DAVIDSON, W. A., and BRODIE, J. (1944) *J. Hyg. Camb.*, 43, 219.
ELKINGTON, G. W., WILSON, G. S., TAYLOR, JOAN, and FULTON, F. (1940) *Brit. med. J.* (i), 477
FELIX, A. (1943) *Brit. med. J.* (i), 435.
——, and CALLOW, B. R. (1943) *Brit. med. J.* (ii), 127.
FISK, R. T. (1942) *J. infect. Dis.*, 71, 153.
GILMAN, B. B., and ANDERSON, G. W. (1938) *Amer.·J. Hyg.*, 28, 345.
HOBBS, BETTY C. (1944) *Monthly Bull. Min. Hlth. and Emerg. Publ. Hlth. Lab. Service*, 3, 11.
HUTCHINSON, J. R. (1943) *Brit. med. J.* (ii), 130.
PICKLES, W. N. (1939) Epidemiology in Country Practice, Bristol.
SMILLIE, W. G., and JEWETT, OLGA F. (1940) *Amer. J. Hyg.*, 32, 79.

Captain John A. Degan, U.S.A.M.C.: In answer to the Chairman's question and speaking purely in terms of my own experience, the problem of how to teach epidemiology to the medical student and young physician has not as yet been solved any more successfully in the United States than in England. As epidemiologist for the American Red Cross—Harvard Unit before entering the Army, I had the privilege of a fairly close association with the Ministry of Health and of visiting and working with a number of local

typhoid outbreak due to type D₁ organisms (Bradley, 1943) and for paratyphoid infections by Hutchinson (1943).

(e) The serological differentiation of Salmonella types has added to our knowledge of the distribution of these bacteria among animals and the channels of spread to man. At the same time the importance of toxins of bacteria other than Salmonella organisms in causing outbreaks of acute gastro-enteritis has been receiving increased attention.

(f) Laboratory methods for identifying strains of bacterial species promise to prove useful in epidemiological inquiry into infection with other kinds of bacteria. In the January number of the Monthly Bulletin an account of two staphylococcal outbreaks was published from Cardiff in which both serological typing and bacteriophage typing (Fisk, 1942) was used to trace the probable sources of infection (Hobbs, 1944).

The techniques used in the study of viruses are of a special kind, not within the scope of the ordinary public health laboratory. Nevertheless the laboratory has given valuable assistance in the study of certain virus infections such as epidemic influenza, smallpox, psittacosis, lymphocytic choriomeningitis and yellow fever; extensions of our knowledge in this field and its application to the study of epidemic disease are required and are certain to be forthcoming.

The Organization of Laboratory Services to Assist in Epidemiological Inquiries

The Emergency Public Health Laboratory Service came into operation in 1939 to meet the threat of epidemic disease which the circumstances of war might favour. Although we have been fortunately free from the increased prevalence of epidemics which was anticipated, I think that the work of this Service has been generally appreciated.

The laboratories were at first situated in rural areas whose population was expected to increase by evacuation from the large towns. Many of these areas did not have their own public health laboratory and from many of them specimens had previously been sent to laboratories at a distance—e.g. from some parts of Wales to London. This of course involved unavoidable delay in transit of specimens and lack of personal contact between the bacteriologist and the local medical officers of health. Furthermore the placing of Emergency Public Health Laboratories in rural areas has the advantage that in such areas, as Pickles has emphasized, outbreaks are more susceptible to detailed inquiry than in the large towns where channels of spread are more difficult to follow. Where special examinations are required involving technical methods beyond the resources of the ordinary laboratory of the Emergency Public Health Laboratory Service, facilities are made available through the co-operation of reference laboratories where such examinations can be made. Moreover the organization of the scattered laboratories into a unified service facilitates interchange and temporary increase of staff as circumstances require. By regular meetings at headquarters and in the regions, by circulation of journals and regular laboratory returns and through the Monthly Bulletin, bacteriologists are kept fully informed of recent work and improvements in technical methods. By the co-operation of many laboratories it has been possible to organize surveys from widely dispersed areas to add to our bacteriological knowledge of epidemic disease. Information of epidemiological interest has been passed quickly to headquarters where close liaison with the Ministry of Health is maintained. In this way the reports from the laboratories can be correlated centrally with information coming to the Ministry through the usual channels.

All these features are worth preserving in a well-organized National Laboratory Service but one matter in the administration of the Emergency Public Health Laboratory Service has not been mentioned. The system of payment by local authorities for work done on a fee-per-specimen basis is avoided. The importance of this policy in whatever Public Health Laboratory Service may be developed in the new health programme is obvious.

The constituent laboratories of the Emergency Public Health Laboratory Service serve the needs of only a small part of the population. Many public health laboratories in existence before the war became associated with the Emergency Public Health Laboratory Service and enjoy such advantages as association with the Service entails. The co-operation of the public health laboratories of the Emergency Pathological Service in the London sectors has also facilitated the central collection of information from the laboratories concerning the distribution and spread of infectious diseases. In any future service, new laboratories will be required to make generally available the assistance which the Emergency Public Health Laboratory Service and associated laboratories have given during the war and the co-operation of more existing laboratories concerned with the diagnosis of infectious disease will be necessary. The first warning of an impending outbreak will not infrequently come from a general hospital laboratory. Under present arrangements the hospital pathologist may notify the public health laboratory of positive

Section of Medicine

President—GEOFFREY EVANS, M.D., F.R.C.P.

[*March* 28, 1944]

Penicillin in the Treatment of Syphilis

By Major C. R. WISE, U.S.A.M.C., & Colonel D. M. PILLSBURY, U.S.A.M.C.

ON the basis of the observation by Mahoney that penicillin has marked spirocheticidal effects in both rabbit and human syphilis, a study of penicillin therapy in 15 patients with early syphilis was recently undertaken at the 2nd General Hospital, U.S. Army. This report will deal only with the immediate effects of treatment, inasmuch as insufficient time has elapsed to allow any conclusions as to the rate of reversal of the blood serologic test for syphilis (STS) or of the eventual outcome as to cure of syphilis in these patients. The patients selected were from non-combat units, in order that adequate follow-up studies could be assured.

The types of syphilis present were as follows: 3 sero-negative primary, 8 sero-positive primary, and 4 secondary. 13 patients had lesions from which *Treponema pallida* could be demonstrated, and the rate of disappearance of treponemata was determined by examinations made at intervals of two hours during the initial day of treatment.

Two schedules of treatment were employed: 5 patients received an injection of 20,000 units of penicillin intramuscularly every four hours, night and day, until a total of 1,000,000 units had been given over a period of just over eight days; 10 patients received an injection of 20,000 units of penicillin every four hours until a total of 500,000 units had been given over a period of four days.

The immediate effects of treatment may be summarized briefly:—

Herxheimer reaction.—Two of the 15 patients had brisk Herxheimer reactions. consisting of fever of 103° and 101° F., respectively, between eight and twelve hours after the initial injection of penicillin. In both of these patients there was marked accentuation of the presenting lesions of syphilis, in one patient a maculo-papular eruption on the trunk, in the other a chancre of the lip. Seven patients had oral temperatures of 100° F. within twelve hours after the initial injection; 6 patients had no fever. None of the reactions noted interfered with continuance of treatment.

Disappearance of Tr. pallida.—The presenting lesions of syphilis became negative for spirochetes of syphilis within fourteen hours in 12 of the 13 patients in whom serial examinations were done. Spirochetes were recovered from one patient fourteen hours after treatment was started; they were not present when the next examination was done ten hours later.

Healing of lesions.—All types of lesions, including clean and secondarily infected chancres, macular and papular secondary lesions, and peri-anal condylomata, healed more quickly than after Mapharsen (Mapharside) therapy. Using the rate of epithelization as a criterion of healing, the time required varied from three to seven days, with a mean of between four and five days. Satellite lymphadenopathy subsided more slowly. The rapidity with which lesions of early syphilis melted away was striking and impressive.

Blood serologic tests.—Quantitative Kahn tests were done daily or every other day during the period of observation in the hospital. There were no changes which could be regarded as outside the limits of error of this method of determining the amount of

JULY—

authorities, and have been most favourably impressed with both the personnel and the technique of epidemiological investigations.

Dr. James A. Doull (Western Reserve University, Cleveland, Ohio): It was in London that the greatest of all field studies was made, namely the demonstration by Dr. John Snow of the relationship between mortality from cholera and consumption of polluted water.

Although all inquiries of this type are designed to elicit new facts relating to sources of infection, modes of transfer, or variations in resistance, field studies may be divided into two classes, according to the conditions under which they are undertaken. First are those of an urgent nature in which the immediate control of an outbreak is necessary, and second, those which are planned in advance and executed at leisure. The latter are broader in scope since they include to-day investigations of tuberculosis, leprosy and other diseases which ordinarily do not occur in epidemic form.

Regarding the machinery for epidemiological study, there is a tendency towards centralization in this as in other fields. Admittedly this has advantages particularly during epidemics. A central authority can maintain experts and advisers, large and well-equipped laboratories and correlate data obtained from the whole area involved. In the United States we must recognize these facts and the National Public Health Service has made notable contributions quite beyond the scope of any State or local health department.

At the same time too great centralization can have a stifling effect. Most of our State health departments, and those of many large cities and counties have full-time epidemiologists and maintain laboratories and other facilities adequate for field research of a very important nature. These organizations, in fact, owe such service to the public, because they hold a monopoly of the essential data, that is, of notifications. The studies of Dr. Chapin, for many years Health Officer of Providence, R.I., serve as sufficient illustration of what can be accomplished by brilliant and persevering efforts, and, I may add, that it is only by offering opportunity for scientific work in epidemiology and related branches that we can hope to attract the highest type of men into public health work.

Dr. J. L. Burn (Salford): In the majority of areas, sanitary inspectors conduct routine epidemiological inquiries. Owing to the shift of emphasis from a traditional view (exemplified by the phrase " drains cause diphtheria ") to the importance of the role of " carriers " and personal contact as factors in the spread of disease, health visitors—carefully chosen and instructed—could now do this work very well.

A health visitor is better suited than the sanitary inspector to examine contacts, to perform technical procedures (such as immunization of contacts against diphtheria) where necessary and to " follow-up " convalescent cases and carriers. Thorough follow-up is a much-neglected field of work, yet one that can be most fruitful. Schedules or model forms for epidemiological inquiries might be compiled by the Ministry of Health on similar lines to the suggestions contained in the circular on food poisoning.

Dr. J. M. Alston (London): In this discussion on a very wide subject, a great deal of emphasis has been put on one aspect only of epidemiological study, namely the identification of bacteria by species and, with more refinement, by types. This by itself is often very useful in showing the source of an outbreak from either certain materials or certain people. But it is only one element in epidemiology and tends to ignore the problem of endogenous infection and of external influences, either local or world-wide, which may have effects in developing foci of infection in different places at about the same time. For example, in influenza epidemics, such as that of a few months ago, there was a tendency to consider that the illness occurred first in one certain place, say in a certain town in the United States and then, by means of an unbroken series of human links, crossed State boundaries, oceans and continents. It cannot be considered adequately proved that such a method of direct transfer is possible in the rapid spread observed and it seems quite likely that for reasons unknown, separate foci arise at about the same time in different places. In that case how many independent foci should we suppose —one in each State or each town or each household? As regards administration of such studies I believe, like Dr. Doull, that an organization in which most individual workers are for much of their time working under central direction is not very likely to be sufficiently original and that a number of separate foci of initiative co-operating in information and experience is very much better.

The inhibitory metabolite analogue should have a structure resembling the natural metabolite so closely that it would have very similar physical constants and thus be an effective competitor in its specific enzyme reaction; and at the same time be sufficiently different chemically for this enzyme reaction to be unable to employ the metabolite analogue effectively. Other ways of inhibiting enzyme reactions are of course possible but cannot be considered here.

Two points immediately arise: (a) How to find and choose the required essential metabolite; (b) how to model the chemical structure of the drug so that it shall reach the target and interfere with that vital process in which 'the chosen essential metabolite is normally used.

There is much evidence which suggests that the substances collectively called growth factors, which have been found to be essential nutrients for one or more species of bacteria, are in fact substances which are essential in the metabolism of a much wider range of organisms. The reason why certain of these substances appear to be essential nutrients for certain species is that these species are unable to synthesize these substances for themselves. Since they are essential to the metabolism of these species, the substances must be acquired preformed from the nutrient environment, just as the vitamins of animal nutrition must be supplied by the food.

The point that these substances, discovered to be essential nutrients for certain bacteria, are really members of a much wider class of essential metabolites required by a large range of organisms, is emphasized by the observation that, in all these cases where examination has been made, bacteria which *do not require to be given one or other of* these growth factors as an essential nutrient, do in fact synthesize these substances.

To summarize: The discovery of essential growth factors or essential nutrients is one way for discovering substances which are components of essential metabolic processes. A mere recital of some of the known bacterial growth factors will show that these substances are common to a very wide range of living organisms. Thus: Aneurin (vitamin B_1); riboflavin (vitamin B_2): nicotinic acid; pantothenic acid; biotin; pyridoxin (vitamin B_6). Each of these has been found to be an essential nutrient for certain species of bacteria, yeasts, moulds, and higher animals. In general there is evidence which suggests that there is a biochemistry which is common to widely different forms of living matter, and which is expressed in the use of common metabolic reactions *in their life processes.*

Thus the whole range of growth factors, of which more are known at present for *micro-organisms* than for higher animals, can assist in making specific the targets in bacteria and other disease-producing micro-organisms at which drugs can be aimed, since even if we do not know what are the metabolic reactions in which these growth *factors* take part we at least know that these substances are essential components of these vital reactions.

Other sulphanilyl drugs such as sulphapyridine, sulphathiazole, sulphadiazine, sulpha-guanidine—are all chemical variants of the same fundamental p-aminobenzene sulphona-mide structure as in sulphanilamide, and their actions all appear to be directed primarily to interference with the p-aminobenzoic acid enzyme system. The bacteriostatic effects of all these sulphanilyl drugs can be abolished by p-aminobenzoic acid. Differences of activity among these related sulphanilyl derivatives appear to be quantitative rather than qualitative. They are probably due mainly to the somewhat different physical constants which the variations in chemical structure impart, thus making them more or less similar in effect to the master compound p-aminobenzoic acid, in regard to the molecular forces in play at the enzyme locus where the normal *substrate* p-amino-benzoic acid would be used.

A number of bacterial growth inhibitors has been prepared following the theory that growth inhibitors can be designed by a reference to the structure of known essential metabolites. Thus, pyridine-3-sulphonic acid or its amide inhibits certain bacteria which require nicotinic acid, i.e. pyridine-3-carboxylic acid, the inhibition being reversed by nicotinic acid or its amide (McIlwain, 1940).

Certain bacteria which require pantothenic acid can be inhibited by pantoyltaurine, the sulphonamide analogue of pantothenic acid; this inhibition is reversed by pantothenic acid (Snell, 1941; McIlwain, 1942; Barnett and Robinson, 1942). Pyrithiamin, in which the thiazole ring of thiamin (aneurin) is changed for a pyridine ring, showed inhibitory effects which were reversed by thiamin (aneurin) (Woolley and White, 1943). One further example is the inhibitory effect of a-amino-sulphonic acid analogues of

syphilis reagin, but it is felt that administration of penicillin probably has the effect of increasing the Kahn titre during the first week of treatment in patients with early syphilis. Following completion of treatment, Kahn tests are being taken at weekly intervals on all patients. In five patients who had a positive STS at the beginning of treatment, and who have now been followed for five weeks, the STS has become negative. This is in accord with Mahoney's observation in four patients, that the STS became negative in from four to seven weeks after administration of 1,280,000 units of penicillin over a period of eight and one-half days.

SUMMARY

Penicillin has a strikingly beneficial effect in the treatment of early syphilis. In our small series, the rate of disappearance of spirochetes and the healing of early lesions were both more rapid than that observed after arsphenamine therapy, either of the conservative or intensive type. The absence of reactions to treatment, and the short time during which treatment may be compressed, make this method of treatment of great potential value in military medicine. Prolonged arsphenamine bismuth therapy for syphilis is unsatisfactory at best, and under conditions of war the difficulties of carrying it out regularly may at times be insurmountable. Intensive therapy offers the advantage of assuring the patient of completion of treatment and prospect of cure in 85 to 90 per cent. of patients, but requires hospitalization for twenty- to twenty-five days, and must be given under expert direction if undue reactions to treatment are to be avoided. The immediate effects of penicillin are greatly superior, and it is hoped that the initial promise of this method will be confirmed by the extensive studies now proceeding in the United States and elsewhere.

Some Aspects of Bacterial Metabolism in Relation to Chemotherapy

By B. C. J. G. KNIGHT, D.Sc. [*in absentia*]

(*The Wellcome Physiological Research Laboratories, Beckenham*)

THE antibacterial drugs of the sulphanilyl group, beginning with prontosil and sulphanilamide, were evolved without knowledge of the target to be attacked within the disease-producing bacteria. But the introduction of these drugs took place at a time when great advances had been made in our knowledge of bacterial biochemistry. A turning point came when it was shown by Woods (1940) that p-aminobenzoic acid was a specific antagonist of bacterial growth-inhibitions caused by sulphanilamide. This observation directly linked the growth-inhibitory effects of the antibacterial drug with the growth processes of the bacterial parasite in a way which threw unexpected light on the target in the parasite at which the drug should be aimed—namely its metabolic processes. The chemical relation between the drug sulphanilamide, i.e. p-aminobenzene sulphonamide and its natural antagonist p-aminobenzoic acid, is very striking, the drug having a sulphonamide group in place of the carboxyl group of its antagonist. Woods suggested that p-aminobenzoic acid itself was really an important metabolite for the streptococci with which he was working, and that it was the normal utilization of this essential metabolite with which the sulphanilamide interfered. Soon after, p-aminobenzoic acid was indeed found to be an essential growth factor for several different species of bacteria, as Woods had predicted (Rubbo and Gillespie, 1940; Lampen and Peterson, 1941; Lampen, Underkofler and Peterson, 1942). This substance is now recognized as an essential metabolite for many bacterial species as well as for other types of organism. Woods showed that the relation of sulphanilamide to p-aminobenzoic acid in his case was analogous to that found in the competitive inhibition of an enzyme reaction. This suggested that the sulphanilamide competed with p-aminobenzoic acid in the utilization of the latter by an enzyme system of the bacterial cell for which p-aminobenzoic acid was the normal substrate, this enzyme reaction being essential for the growth of the bacterial cell.

The generalization which followed from this was put forward by Fildes (1940) namely, that bacteriostatic substances could be designed deliberately to interfere with metabolic reactions which were essential to the growth of the bacteria it was desired to inhibit, by making the inhibitor to have a chemical structure related to, but sufficiently different from, one of the essential metabolites of the cell. The drug might then be expected to interfere with the use of the normal metabolite, by some form of enzyme inhibition.

often relates to the cells' powers of synthesis. In regard to a given essential metabolite some species may be able to synthesize it quite easily. Other species will be unable to synthesize it sufficiently rapidly, and must be given it as a nutrient. Similar differences may occur between different strains of the same species. Merely different rates of synthesis of an essential metabolite could give rise to different results from a drug acting on the different strains, since these strains would be capable of producing the natural antagonist of the drug at different rates.

It is possible to train nutritionally exacting strains of bacteria to become less exacting by becoming faster synthesizers of a metabolite which they ordinarily acquire preformed from their nutrients. One of the ways of doing this is continued sub-culture under sub-optimal nutrient conditions (e.g. Koser and Wright, 1943). In the case of drug resistance this can be done by sub-culture in somewhat less than bacteriostatic concentrations of the drug (McIlwain, 1943a). Here the drug, as a metabolite inhibitor, is partially blocking the use of the normal metabolite, thus causing a partial starvation to which the bacterial cell can respond by an increased rate of synthesis of the natural metabolite. This adapted strain will then need higher concentrations of drug to inhibit it. These concentrations may be outside the practical range in treatment. In certain cases it has been shown that bacteria rendered resistant to drugs of the sulphanilyl group did in fact synthesize more p-aminobenzoic acid than did the normal sensitive strains (Landy, Larkum, Oswald and Streightoff 1943; McIlwain 1943a).

This drug resistance, due to an increased rate of synthesis of the natural drug antagonist (i.e. the normal essential metabolite) once acquired, can persist through subsequent sub-cultures in varying degrees. To avoid the conditions of exposure to sub-bacteriostatic concentrations of drug which could give rise in this way to drug-tolerant strains, is an important reason for avoiding prolonged treatment with small doses of drug. Once a strain has been made tolerant to one member of the sulphanilyl group, it will be tolerant also to the other members of this group if its tolerance is due to its having acquired a greater power to synthesize p-aminobenzoic acid, or is otherwise related to p-amino-benzoic acid metabolism.

Such a strain might then usefully be attacked by an inhibitor modelled on another essential metabolite, such as pantoyltaurine as McIlwain and Hawking suggested, since the strain will not have been trained to synthesize pantothenic acid at an enhanced rate by cultivation in the presence of a p-aminobenzoic acid inhibitor.

Another way in which a drug-tolerant strain might arise is theoretically possible. This is when the bacterial cells respond to the drug, not by an increased production of the corresponding natural metabolite, but by using a new series of metabolite reactions which have the effect of by-passing the reaction stage which the inhibitor is blocking. It must also be remembered that the infecting organisms may not be a nutritionally pure culture, so that selection of a strain best able to cope with the given nutritional environment, which will include the drug, may also occur.

A secondary effect of the use of drugs modelled on essential metabolites is the effect of the drug on the nutrition of the host. Although p-aminobenzoic acid is not yet generally accepted as a vitamin of human nutrition, there is reason to believe that this substance does play a part in human metabolism, so that prolonged use of a drug of the sulphanilyl group might interfere with the p-aminobenzoic acid mechanism of the host.

A further, more, general nutritional derangement also could follow from the effect of the drug on the bacterial flora of the intestines. Since it seems probable that the bacteria of the intestines synthesize vitamins which are used in the nutrition of the host, a radical change in this flora produced by drug treatment might result in smaller quantities of vitamins becoming available to the host from this source. The point emerges that the successful chemotherapeutic treatment itself may cause temporary nutritional deficiencies in the host. These could be remedied by suitable vitamin supplements during convalescence.

NATURAL ANTIBIOTICS

Finally, turning briefly to the naturally occurring antibiotics, of which penicillin is outstanding, there is very little that can be said at present from the point of view of bacterial metabolism. Penicillin is only one case in many, in which a metabolic product of one species of micro-organism is antagonistic to the growth of other species. Numerous other examples of antagonism between bacterial species due to the production of inhibitory substances are known, for example, gramicidin, tyrocidin, and streptothricin. The existence of these substances produced by the flora of the soil opens interesting problems of soil ecology. It would be tempting to see in these substances the evolution of protective substances for the particular species which produce them. But this may be a

certain simple α-amino-carboxylic acids (glycine, alanine, etc.) which were required as nutrients by certain bacteria (McIlwain, 1941).

Thus there is no lack of evidence that growth inhibitors can be prepared by modelling them on the known essential metabolites.

EFFECTS DUE TO THE HOST

How effective such compounds might be when used *in vivo* will depend in the first instance on the usual relation between effect on the parasite and on the host. Because, as is clear, the essential metabolites themselves are, in all the cases mentioned, also essential for the host animal, including man.

Using pantoyltaurine, McIlwain and Hawking (1943) were able to afford protection to rats against large attacking doses of hæmolytic streptococci, but a similar protection could not be afforded to mice. The mice had in their blood a higher concentration of pantothenate (the natural essential metabolite) than had the rats. Injected pantoyltaurine was unable to produce a high enough ratio of pantoyltaurine to pantothenate to bring about bacteriostasis in the mice. In the rat blood, the pantothenate concentration was low enough for injected pantoyltaurine to be able to maintain the pantoyltaurine/pantothenate ratio large enough to produce a bacteriostasis. This ratio agreed with that expected from *in vitro* experiments. Thus the concentration of a given essential metabolite in the host can effect the result of the use of its corresponding inhibitory analogue against a parasite in that host.

The same drug might thus have apparently different effectiveness against the same parasite in different species of host. But this could also clearly apply to different individuals of the same species, depending on their nutritional conditions. Thus, one human subject, suffering from a nutritional p-aminobenzoic acid deficiency, might show a better response in treatment with sulphathiazole or other sulphanilyl derivative than another human subject who, because of a different diet or for other reasons, had much more free p-aminobenzoate in his tissues or blood, even though the attacking organisms were from the same culture, or showed the same sensitivity *in vitro*.

Thus in general, individual hosts might show different effects in treatment by the same drug, due to differences in the concentration of the drug's natural antagonist. A natural antagonist will always be present in the host in all the cases where the growth inhibitor is modelled on an essential metabolite.

RELATION OF CHEMICAL STRUCTURES OF METABOLITE AND INHIBITOR

Of the five groups of inhibitors modelled on essential metabolites just mentioned, four of them contain sulphonamide groups in place of a carboxyl group in the natural metabolite. It is clear that this sulphonamide group sufficiently resembles the carboxyl group in its physical constants to be a very close substitute in this respect (cf. Bell and Roblin, 1942; Kumler and Daniels, 1943). It thus permits effective competition in the enzyme systems which normally use the natural metabolite. Further, this sulphonamide group, in spite of its close resemblance to the carboxyl group, is sufficiently unusual chemically for the enzymes of the cells neither to be able to use it instead of the carboxyl group (because it cannot participate in the normal series of chemical reactions required) nor to be able to split it off easily and thus render the molecule an ineffective competitor. The case of pyrithiamin shows however that the sulphonamide group itself cannot be looked upon as a toxic group of the molecule in the old chemotherapeutic sense since here an inhibitor is modelled without a sulphonamide group. Doubtless inhibitors which might be modelled on other essential metabolites, such as riboflavin or pyridoxin, which do not contain carboxyl groups, might require groups other than sulphonamide groups to enable them to make effective contact with an appropriate enzyme system while not being chemically usable by it.

DRUG TOLERANCE

An important property of bacterial cells, which can cause difficulties in using drugs which inhibit essential metabolic reactions, is that of metabolic adaptability, which can give rise to drug-resistant strains. The synthetic powers of bacteria are by no means so fixed as they become in higher types of organism which have evolved a well-defined apparatus of genetic control of their biochemical processes. In bacteria the mechanisms that determine how closely daughter-cells shall resemble the parent cell are much less insulated from the environment than these mechanisms become when more evolved and more clearly differentiated. Thus, phenomena of adaptation in response to environmental conditions are often found with bacteria and this adaptability

often relates to the cells' powers of synthesis. In regard to a given essential metabolite some species may be able to synthesize it quite easily. Other species will be unable to synthesize it sufficiently rapidly, and must be given it as a nutrient. Similar differences may occur between different strains of the same species. Merely different rates of synthesis of an essential metabolite could give rise to different results from a drug acting on the different strains, since these strains would be capable of producing the natural antagonist of the drug at different rates.

It is possible to train nutritionally exacting strains of bacteria to become less exacting by becoming faster synthesizers of a metabolite which they ordinarily acquire preformed from their nutrients. One of the ways of doing this is continued sub-culture under sub-optimal nutrient conditions (e.g. Koser and Wright, 1943). In the case of drug resistance this can be done by sub-culture in somewhat less than bacteriostatic concentrations of the drug (McIlwain, 1943a). Here the drug, as a metabolite inhibitor, is partially blocking the use of the normal metabolite, thus causing a partial starvation to which the bacterial cell can respond by an increased rate of synthesis of the natural metabolite. This adapted strain will then need higher concentrations of drug to inhibit it. These concentrations may be outside the practical range in treatment. In certain cases it has been shown that bacteria rendered resistant to drugs of the sulphanilyl group did in fact synthesize more p-aminobenzoic acid than did the normal sensitive strains (Landy, Larkum, Oswald and Streightoff 1943; McIlwain 1943a).

This drug resistance, due to an increased rate of synthesis of the natural drug antagonist (i.e. the normal essential metabolite) once acquired, can persist through subsequent sub-cultures in varying degrees. To avoid the *conditions of exposure to sub-bacteriostatic* concentrations of drug which could give rise in this way to drug-tolerant strains, is an important reason for avoiding prolonged treatment with small doses of drug. Once a strain has been made tolerant to one member of the sulphanilyl group, it will be tolerant also to the other members of this group if its tolerance is due to its having acquired a greater power to synthesize p-aminobenzoic acid, or is otherwise related to p-amino-benzoic acid metabolism.

Such a strain might then usefully be attacked by an inhibitor modelled on another essential metabolite, such as pantoyltaurine as McIlwain and Hawking suggested, since the strain will not have been trained to synthesize pantothenic acid at an enhanced rate by cultivation in the presence of a p-aminobenzoic acid inhibitor.

Another way in which a drug-tolerant strain might arise is theoretically possible. This is when the bacterial cells respond to the drug, not by an increased production of the corresponding natural metabolite, but by using a new series of metabolite reactions which have the effect of by-passing the reaction stage which the inhibitor is blocking. It must also be remembered that the infecting organisms may not be a nutritionally pure culture, so that selection of a strain best able to cope with the given nutritional environment, which will include the drug, may also occur.

A secondary effect of the use of drugs modelled on essential metabolites is the effect of the drug on the nutrition of the host. Although p-aminobenzoic acid is not yet generally accepted as a vitamin of human nutrition, there is reason to believe that this substance does play a part in human metabolism, so that prolonged use of a drug of the sulphanilyl group might interfere with the p-aminobenzoic acid mechanism of the host.

A further, more, general nutritional derangement also could follow from the effect of the drug on the bacterial flora of the intestines. Since it seems probable that the bacteria of the intestines synthesize vitamins which are used in the nutrition of the host, a radical change in this flora produced by drug treatment might result in smaller quantities of vitamins becoming available to the host from this source. The point emerges that the successful chemotherapeutic treatment itself may cause temporary nutritional deficiencies in the host. These could be remedied by suitable vitamin supplements during convalescence.

NATURAL ANTIBIOTICS

Finally, turning briefly to the naturally occurring antibiotics, of which penicillin is outstanding, there is very little that can be said at present from the point of view of bacterial metabolism. Penicillin is only one case in many, in which a metabolic product of one species of micro-organism is antagonistic to the growth of other species. Numerous other examples of antagonism between bacterial species due to the production of inhibitory substances are known, for example, gramicidin, tyrocidin, and streptothricin. The existence of these substances produced by the flora of the soil opens interesting problems of soil ecology. It would be tempting to see in these substances the evolution of protective substances for the particular species which produce them. But this may be a

certain simple α-amino-carboxylic acids (glycine, alanine, etc.) which were required as nutrients by certain bacteria (McIlwain, 1941).

Thus there is no lack of evidence that growth inhibitors can be prepared by modelling them on the known essential metabolites.

EFFECTS DUE TO THE HOST

How effective such compounds might be when used *in vivo* will depend in the first instance on the usual relation between effect on the parasite and on the host. Because, as is clear, the essential metabolites themselves are, in all the cases mentioned, also essential for the host animal, including man.

Using pantoyltaurine, McIlwain and Hawking (1943) were able to afford protection to rats against large attacking doses of hæmolytic streptococci, but a similar protection could not be afforded to mice. The mice had in their blood a higher concentration of pantothenate (the natural essential metabolite) than had the rats. Injected pantoyltaurine was unable to produce a high enough ratio of pantoyltaurine to pantothenate to bring about bacteriostasis in the mice. In the rat blood, the pantothenate concentration was low enough for injected pantoyltaurine to be able to maintain the pantoyltaurine/pantothenate ratio large enough to produce a bacteriostasis. This ratio agreed with that expected from *in vitro* experiments. Thus the concentration of a given essential metabolite in the host can effect the result of the use of its corresponding inhibitory analogue against a parasite in that host.

The same drug might thus have apparently different effectiveness against the same parasite in different species of host. But this could also clearly apply to different individuals of the same species, depending on their nutritional conditions. Thus, one human subject, suffering from a nutritional p-aminobenzoic acid deficiency, might show a better response in treatment with sulphathiazole or other sulphanilyl derivative than another human subject who, because of a different diet or for other reasons, had much more free p-aminobenzoate in his tissues or blood, even though the attacking organisms were from the same culture, or showed the same sensitivity *in vitro*.

Thus in general, individual hosts might show different effects in treatment by the same drug, due to differences in the concentration of the drug's natural antagonist. A natural antagonist will always be present in the host in all the cases where the growth inhibitor is modelled on an essential metabolite.

RELATION OF CHEMICAL STRUCTURES OF METABOLITE AND INHIBITOR

Of the five groups of inhibitors modelled on essential metabolites just mentioned, four of them contain sulphonamide groups in place of a carboxyl group in the natural metabolite. It is clear that this sulphonamide group sufficiently resembles the carboxyl group in its physical constants to be a very close substitute in this respect (cf. Bell and Roblin, 1942; Kumler and Daniels, 1943). It thus permits effective competition in the enzyme systems which normally use the natural metabolite. Further, this sulphonamide group, in spite of its close resemblance to the carboxyl group, is sufficiently unusual chemically for the enzymes of the cells neither to be able to use it instead of the carboxyl group (because it cannot participate in the normal series of chemical reactions required) nor to be able to split it off easily and thus render the molecule an ineffective competitor. The case of pyrithiamin shows however that the sulphonamide group itself cannot be looked upon as a toxic group of the molecule in the old chemotherapeutic sense since here an inhibitor is modelled without a sulphonamide group. Doubtless inhibitors which might be modelled on other essential metabolites, such as riboflavin or pyridoxin, which do not contain carboxyl groups, might require groups other than sulphonamide groups to enable them to make effective contact with an appropriate enzyme system while not being chemically usable by it.

DRUG TOLERANCE

An important property of bacterial cells, which can cause difficulties in using drugs which inhibit essential metabolic reactions, is that of metabolic adaptability, which can give rise to drug-resistant strains. The synthetic powers of bacteria are by no means so fixed as they become in higher types of organism which have evolved a well-defined apparatus of genetic control of their biochemical processes. In bacteria the mechanisms that determine how closely daughter-cells shall resemble the parent cell are much less insulated from the environment than these mechanisms become when more evolved and more clearly differentiated. Thus, phenomena of adaptation in response to environmental conditions are often found with bacteria and this adaptability

Clinical Section

President—J. D. Rolleston, M.D.

[*February 11, 1944*]

Meeting at St. Mary's Hospital, London, W.2

Three Cases shown by Duncan C. L. Fitzwilliams, C.M.G., F.R.C.S.

(1) Fore-Quarter Amputation for Carcinoma of the Axillary Tail of the Breast.

Mrs. B., aged 42.

History.—Found to have lump under right arm August 1940. This eventually incised as a "cold abscess". Later had second operation leaving a discharging area; wound having healed, deep X-ray therapy prescribed and subsequently small doses of radium.

On examination (19.8.43).—Discharging crater in right axilla. Carcinoma of axillary tail. Circumference of arms, R. 13 in., L. 10 in. Interstitial radium 7,776 mg. hrs. given to the area followed at once by 1,920 mg. hrs. of surface radiation. Stilbœstrol not tolerated. H. 11 prescribed and pain controlled by morphia.

Area improved but swelling of right arm increased and patient decided to have fore-quarter amputation performed. Operation done January 10, 1944. Recovery satisfactory and subsequent progress uneventful.

Author's note.—This case is unique in that the woman still has an intact breast on the side of a fore-quarter amputation.

(2) Carcinoma. ? Metastasis or New Growth.

Miss. J., aged 41.

March 1931, when 27 years old, patient had radical removal of left breast for carcinoma, followed by surface radiation. Various small lumps were removed in the ensuing years, and none showed malignancy until July 1943, when a malignant change was found in the right breast. Since then under observation, and in January 1944 nodules removed from the scar of the last operation; on section these proved to be malignant. ? metastasis or a new carcinoma in right breast.

(3) Radium Necrosis Following Old Case of Carcinoma of Breast.

Mrs. M., aged 58.

First seen February 1929 with lump in right axilla—known for one month—obvious carcinoma. This was removed and later in the year she returned—first for a radium course, and then for the removal of a small recurrence.

June 1933 a further recurrence was treated with a large interstitial dose of radium 12,096 mg. hrs. Deep necrosis followed. The area did not heal for four years, and various operations were performed for the removal of dead tissue including portions of two ribs. Since then under constant observation. Early in 1943 hardness of left breast was found and surface radium was given (7,920 mg. hrs.). Late in 1943 remains of the right breast began to show signs of active infection—? recurrence or new carcinoma. Recently left breast treated with interstitial and surface radiation.

Inter-atrial Septal Defect in Mother and Son.—C. G. Barnes, M.D.

E. C., female, aged 37.

Has always become cyanosed and dyspnœic on slight exertion. At age of 27, normal delivery of son. Had small hæmoptyses in 1940 and 1943.

Exercise tolerance increasingly impaired recently, is breathless after walking 50 yards on the level.

much too teleological view of the matter. At present there appears to be no evidence connecting the chemical composition of these natural antibiotics, where known, with any of the essential metabolites already mentioned, except possibly gramicidin with protein synthesis.

The bacterial pigment iodinin, which is a phenazine derivative, has inhibitory effects against streptococci, the inhibition being reversed by various anthraquinone and naphthaquinone derivatives, including synthetic vitamin K substitutes (McIlwain, 1943b). One possible approach to the discovery of the mode of action of natural antibiotics is to seek, in cells which they do not inhibit, possible natural antagonists, which might be expected to be related to the essential reactions with which the antibiotic interfered.

REFERENCES

BARNETT, J., and ROBINSON, F. A. (1942) *Biochem. J.*, **36**, 364.
BELL, P. H., and ROBLIN, Jr., R. O. (1942) *J. Amer. chem. Soc.*, **64**, 2905.
FILDES, P. (1940) *Lancet* (i), 955.
KOSER, S. A., and WRIGHT, M. H. (1943) *J. Bact.*, **46**, 239.
KUMLER, W. D., and DANIELS, T. C. (1943) *J. Amer. chem. Soc.*, **65**, 2190.
LAMPEN, J. O., and PETERSON, W. H. (1941) *J. Amer. chem. Soc.*, **63**, 2283.
LAMPEN, J. O., UNDERKOFLER, L. A., and PETERSON, W. H. (1942) *J. biol. Chem.*, **146**, 277.
LANDY, M., LARKUM, N., OSWALD, E. J., and STREIGHTOFF, F. (1943) *Science* **97**, 265.
McILWAIN, H. (1940) *Brit. J. exp. Path.*, **21**, 136.
——— (1941) *Brit. J. exp. Path.*, **22**, 148.
——— (1942) *Brit. J. exp. Path.*, **23**, 95.
——— (1943a) *Brit. J. exp. Path.* **24**, 203 and 212.
——— (1943b) *Biochem. J.*, **37**, 265.
McILWAIN, H., and HAWKING, F. (1943) *Lancet* (i), 449.
RUBBO, S. D., and GILLESPIE, J. M. (1940) *Nature*, Lond., **146**, 838.
SNELL, E. E. (1941) *J. Biol. Chem.*, **139**, 975; ibid., **141**, 121.
WOODS, D. D. (1940) *Brit. J. exp. Path.*, **21**, 74.
WOOLLEY, D. W., and WHITE, A. G. C. (1943) *J. exp. Med.*, **78** 489.

Essential Hypertension Treated by Splanchnectomy.—A. DICKSON WRIGHT, M.S.

L. J., male, aged 41. While working on the Gold Coast he developed severe occipital headaches, dizziness and some difficulty with his eyes. His work in Africa was very strenuous, and he drank and smoked excessively. At times his blood-pressure went as high as 250/160 and was always over 200 systolic. He became quite incapable of work on account of his symptoms although investigation showed no renal incapacity or retinal hæmorrhages, and operative treatment was decided upon.

On January 17 and 31, 1944, splanchnectomy, lumbar sympathectomy, partial adrenalectomy and decapsulation of the kidneys were performed.

His blood-pressure now is 140/90, his symptoms have all disappeared and he has found fresh employment.

Hypertension Associated with Atrophic Pyelonephritis of One Kidney.—A. DICKSON WRIGHT, M.S.

Mrs. T., aged 38. History of nightmares, headaches and giddiness and a hypertensive family history.

On examination.—Blood-pressure 190/120.

Excretion urography showed right kidney functionless, and ascending pyelography showed this kidney to have a rather dilated pelvis but a grossly shrunken parenchyma.

14.2.44: The kidney was removed and unilateral splanchnectomy done with return of pressure to normal level. The kidney was evidently only diseased in so far as the parenchyma was concerned because the pelvis corresponded in size and configuration to that of the normal kidney but the parenchyma had shrunk down upon the pelvis and showed characteristic fibrotic and arteriolosclerotic changes.

At the present time the patient enjoys splendid health and all her symptoms, even the nightmares, are gone.

[*April* 14, 1944]

DISCUSSION ON CASES TREATED BY PENICILLIN

A. Diseases of the Chest Including Empyemata

Male, aged 38. Hæmolytic Streptococcal Pneumonia and Empyema.—Shown by Staff of St. Mary's Hospital.

Three Cases of Empyema treated by Local Application only of Calcium Salt of Penicillin in Normal Saline. Treatment at University College Hospital. Shown by R. S. PILCHER, M.S.

(1) P. B., female, aged 18. Synpneumonic Left Empyema.
(2) K. W., male, aged 19. Right Empyema After "Flu."
(3) H. H., male, aged 44. Left Empyema After Pneumonectomy for Bronchiectasis.

Four Cases Illustrating the Treatment of Empyemata by Injection of Penicillin into the Pleural Cavity.—K. M. A. PERRY, M.D., and E. C. B. BUTLER, F.R.C.S.

(1) Male, aged 10. Pneumococcal Pneumonia. Left Empyema.
(2) Female, aged 71. Right Pneumococcal Empyema.
(3) Female, aged 60. Right Pneumococcal Empyema.
(4) Male, aged 53. Right Streptococcal Empyema.

Professor R. S. Pilcher: It is possible to sterilize the pleura by local application of penicillin, provided that the organisms are sensitive and the drug has access to the whole cavity. There are two possible sources of reinfection, a bronchial fistula and the channel by which the drug is given. The latter is within our control but needs emphasis for penicillin is already undermining the ritual of asepsis and I have no doubt from what I have seen and read that infection with resistant organisms introduced during treatment is spoiling some of the results. Bronchial fistula, if large, will defeat treatment but in one of the foregoing cases a fistula associated with acute empyema seemed to make little difference and it was only in evidence on one occasion.

This sterilizing effect of penicillin is of general interest and the pleura provides a useful test tube for its study but there remains the problem of impairment of respiratory function that follows empyema, whether sterile or infected. It is still important to prevent stiffness of the chest wall and to get the lung expanded as soon as possible (unless it has been removed or is having therapeutic collapse). For this reason the pleura

On examination.—Well developed with slight cyanosis of lips, ears and extremities, more marked after exertion. No clubbing. Heart not enlarged. Regular rhythm. Resting rate 80. Parasternal dullness in second left space. Soft systolic murmur in third left space. Friction rub over pulmonary artery. B.P. 190/100 arms, 210/120 legs. Arm-to-tongue circulation time (Decholin) 13 secs. Blood-count: Hb. 125% (Haldane). R.B.C. 6,200,000 per c.mm.

Electrocardiogram.—Normal sinus rhythm; right axis deviation; P waves of relatively high voltage; S-T segments depressed in Leads II, III and C-R$_1$; T waves inverted in Leads III and C-R$_1$.

X-ray examination (Dr. Rohan Williams).—Heart not enlarged; considerable dilatation of pulmonary artery and its main branches; appearances consistent with presence of inter-atrial defect of patent ductus arteriosus. *Screening.*—Typical hilar dance; no ventricular enlargement.

E. C., male, aged 10 (son of the above).

History of cyanosis and breathlessness on exertion. Systolic murmur in third left space. B.P. 125/70. Fingers not clubbed.

Electrocardiogram.—Sinus arrhythmia and slight degree of right axis deviation.

X-ray examination (Dr. Rohan Williams).—Heart not enlarged; pulmonary artery prominent but no apparent increase in size of peripheral pulmonary vessels; appearances consistent with, but not pathognomonic of, inter-atrial septal defect.

Chronic Gonococcal Arthritis Treated with Penicillin.—J. SUCHET, M.R.C.S., L.R.C.P.

H. D., male, aged 41.

History.—1923: Acute gonorrhœa treated in India—apparently cured. 1940: Acute gonorrhœa treated by own doctor with "tablets". (The female contact attended St. Mary's Hospital and was cured with sulphapyridine). Six weeks later the patient developed acute arthritis of left elbow and subsequently multiple joints were similarly affected. For three and a half years was more or less crippled, spending nearly sixteen months in various hospitals receiving treatment with sulphonamides, heat and short-wave therapy, protein shock and mixed vaccines.

Condition on admission May 14, 1943.—Chronic urethral discharge. Prostate enlarged and tender. Vesicles, epididymides and testicles normal. Both knees acutely swollen and painful with all movements extremely limited. Marked wasting both quadriceps. Both ankles swollen and painful with all movements limited. Left elbow showed periarticular thickening, slightly tender with slight limitation of movement. Toes of both feet acutely swollen and tender.

Investigations.—Temperature 99·8; pulse 112. Urethral discharge: Gonococci in smear. Culture negative. Wassermann reaction negative. Gonococcal complement-fixation test strongly positive. Blood sedimentation rate 64 in one hour (Westergren). X-rays showed rarefaction of bone ends with increase of joint space and some cartilage destruction consistent with acute inflammatory changes upon a chronic condition.

Treatment prior to penicillin: Sulphathiazole, sulphadiazine, protein shock (T.A.B.), and short-wave therapy resulted in gradual improvement but joints relapsed and patient was never fit to leave bed. Urethral discharge disappeared but prostatic bead examinations, while showing no gonococci, gave heavy growths of staphylococci sensitive to penicillin but completely resistant to sulphathiazole.

Penicillin treatment.—300,000 units were administered in eighty-four hours partly by single intravenous and intramuscular injections and also by continuous intravenous drip at different rates. (The penicillin blood levels obtained were illustrated by Prof. Fleming in *Proc. R. Soc. Med.*, 1944, 37, 102, fig. 2.)

Result of penicillin treatment.—On the day following commencement of therapy there was marked diminution of pain. Freedom of movement became gradually noticeably easier and by the end of treatment movement was restricted solely by stiffness, nearly all swelling having resolved. Two days later patient was allowed up and on the fourth day he was walking. With the help of massage and exercises he was walking freely at the end of a week. "For the first time in three and a half years I have been able to walk without sticks."

Improvement continued and patient was discharged three weeks after treatment with penicillin.

Observation has been maintained and during these nine months he has remained perfectly well. He is engaged in full-time work as a lorry driver and there has never been the slightest sign of a relapse. When last seen there were no abnormal physical signs apart from some slight thickening around the elbow-joint.

Essential Hypertension Treated by Splanchnectomy.—A. DICKSON WRIGHT, M.S.

L. J., male, aged 41. While working on the Gold Coast he developed severe occipital headaches, dizziness and some difficulty with his eyes. His work in Africa was very strenuous, and he drank and smoked excessively. At times his blood-pressure went as high as 250/160 and was always over 200 systolic. He became quite incapable of work on account of his symptoms although investigation showed no renal incapacity or retinal hæmorrhages, and operative treatment was decided upon.

On January 17 and 31, 1944, splanchnectomy, lumbar sympathectomy, partial adrenalectomy and decapsulation of the kidneys were performed.

His blood-pressure now is 140/90, his symptoms have all disappeared and he has found fresh employment.

Hypertension Associated with Atrophic Pyelonephritis of One Kidney.—A. DICKSON WRIGHT, M.S.

Mrs. T., aged 38. History of nightmares, headaches and giddiness and a hypertensive family history.

On examination.—Blood-pressure 190/120.

Excretion urography showed right kidney functionless, and ascending pyelography showed this kidney to have a rather dilated pelvis but a grossly shrunken parenchyma.

14.2.44: The kidney was removed and unilateral splanchnectomy done with return of pressure to normal level. The kidney was evidently only diseased in so far as the parenchyma was concerned because the pelvis corresponded in size and configuration to that of the normal kidney but the parenchyma had shrunk down upon the pelvis and showed characteristic fibrotic and arteriolosclerotic changes.

At the present time the patient enjoys splendid health and all her symptoms, even the nightmares, are gone.

[*April* 14, 1944]

DISCUSSION ON CASES TREATED BY PENICILLIN

A. Diseases of the Chest Including Empyemata

Male, aged 38. Hæmolytic Streptococcal Pneumonia and Empyema.—Shown by Staff of St. Mary's Hospital.

Three Cases of Empyema treated by Local Application only of Calcium Salt of Penicillin in Normal Saline. Treatment at University College Hospital. Shown by R. S. PILCHER, M.S.

(1) P. B., female, aged 18. Synpneumonic Left Empyema.
(2) K. W., male, aged 19. Right Empyema After "Flu."
(3) H. H., male, aged 44. Left Empyema After Pneumonectomy for Bronchiectasis.

Four Cases Illustrating the Treatment of Empyemata by Injection of Penicillin into the Pleural Cavity.—K. M. A. PERRY, M.D., and E. C. B. BUTLER, F.R.C.S.

(1) Male, aged 10. Pneumococcal Pneumonia. Left Empyema.
(2) Female, aged 71. Right Pneumococcal Empyema.
(3) Female, aged 60. Right Pneumococcal Empyema.
(4) Male, aged 53. Right Streptococcal Empyema.

Professor R. S. Pilcher : It is possible to sterilize the pleura by local application of penicillin, provided that the organisms are sensitive and the drug has access to the whole cavity. There are two possible sources of reinfection, a bronchial fistula and the channel by which the drug is given. The latter is within our control but needs emphasis for penicillin is already undermining the ritual of asepsis and I have no doubt from what I have seen and read that infection with resistant organisms introduced during treatment is spoiling some of the results. Bronchial fistula, if large, will defeat treatment but in one of the foregoing cases a fistula associated with acute empyema seemed to make little difference and it was only in evidence on one occasion.

This sterilizing effect of penicillin is of general interest and the pleura provides a useful test tube for its study but there remains the problem of impairment of respiratory function that follows empyema, whether sterile or infected. It is still important to prevent stiffness of the chest wall and to get the lung expanded as soon as possible (unless it has been removed or is having therapeutic collapse). For this reason the pleura

must be cleaned out and if necessary a thoracotomy must be done for this purpose. Moreover it must be kept clean by lavage even after the contents have been sterilized. Of two acute empyemas shown at this meeting one has reaccumulated thick sterile pus, the other has not. The former is still under treatment to prevent organization of the exudate. A second reason for the pleural toilet at the start is to break down loculations in the pleura which may prevent the penicillin reaching the whole cavity. In addition to measures aimed at reducing the fibrin content of the exudate the return of function will be improved by breathing exercises. These are of value at all ages but in children their effect is remarkable and quite grotesque postural changes following immobilization of one side of the chest can be fully corrected or better still can be prevented.

We have treated seventeen empyemata to date and no two of them have been alike. We have had several failures, most of them determined by large bronchial fistulæ, and some very striking successes. In particular I might mention two cases of infected therapeutic pneumothorax, one with tension, the other without. At present one can make no rules as to procedure or dosage, but with regard to the latter our experience shows that it is necessary to continue treatment after the fluid becomes sterile and I suggest that a bacteriostatic concentration should be maintained in the pleura for a week.

We have used two techniques for the introduction of penicillin and pleural lavage. Either a stout aspirating needle is used or a fine catheter is put in through an intercostal space. Thoracotomy wounds made for pleural toilet have healed by first intention. At present we are using calcium salt of penicillin in concentration of 1,000 U/c.c. in amounts of 10 to 50 c.c. according to the size of cavity and this seems to give an effective intrapleural concentration for three days.

Whatever the bacteriological results of penicillin, other measures must be taken to prevent loculation, pleural thickening and immobilization of the chest wall.

Dr. K. M. A. Perry: The aims in the treatment of acute empyema are firstly to sterilize the cavity and overcome the toxæmia, and secondly to restore the function of the chest wall. Fourteen cases of empyema have been treated by repeated aspiration of pus and local injection of penicillin, and Tables I and II (p. 501) give details of them. By this method of treatment it is clearly possible to sterilize the cavity, though if it is loculated each locule must be aspirated. Infection may recur if the dosage of penicillin is small, but can be easily dealt with by further injections of the drug. The general condition of the patient is also greatly improved, and the toxæmia overcome.

An important consideration, however, is restoration of function, which would be much impeded by a residual thickened pleura or rigid chest wall. There is much fibrin formed in an empyema cavity, and therefore some thickening is inevitable, even after rib resection. It is necessary to ascertain whether simple aspiration leaves a marked impairment of function; and whether washing out of the cavity at the commencement of treatment is necessary, or whether penicillin can only become an adjuvant to rib resection. An attempt has been made to ascertain what can be hoped for from simple aspiration. It will take considerable time to assess the results with regard to function, and it is too early yet to form a final opinion.

There is certainly considerable thickening and rigidity in the more severe of these cases at the present time: but the lungs are still re-expanding and a great deal can be re-absorbed. In the two ladies, despite the thickening, the result achieved is very satisfactory. It may be that aspiration alone will suffice in the elderly and in children, while rib resection will still be necessary in many adults.

Re-expansion of the lung has always been a problem in the treatment of empyema. It is the principal problem in these patients. It might be achieved more easily if the disease in the lung could be treated at the same time by systemic penicillin, but supplies have not been available for this purpose. We have therefore concentrated on achieving re-expansion by means of breathing exercises.

One of the cases was a secondarily infected tuberculous pyopneumothorax, and this was very satisfactorily sterilized by penicillin. We have also used penicillin in one case to prevent infection in a traumatic hæmothorax.

Mr. A. Dickson Wright: In empyema it is most unusual to have a simple collection of pus in the pleural cavity; there is usually a mixture of fibrin clots and pus resembling curds and whey, and it is asking too much to expect nature and penicillin to deal with this mixture. A revival of Hathaway's treatment of the last war would seem to meet the case; this consists of thoracotomy with a thorough cleaning of the pleural cavity from all fibrin clots free and adherent, then a tight closure of the chest with aspirations for subsequent collections which are never fibrinous.

14 CASES OF EMPYEMA (K. M. A. PERRY).

TABLE I.—DISCHARGED FROM HOSPITAL.

No.	Sex	Age	Side	Complicating disease	Date of admission	Organism	Units of penicillin	Date of discharge	No. of aspirations	Most removed at single aspiration	Present condition
1	M.	55	Right	Perforated appendix	10.9.43	Non-haemolytic streptococcus (secondarily *Cl. welchii*)	40,000	16.10.43	4	18 oz.	Following reconstruction of abdominal wall is now back at work. Little pleural thickening and back to normal activity
2*	F.	60	Right	—	2.10.43	Pneumococcus Type 28	80,000	30.11.43	11	4 oz.	Well. Some thickened pleura anteriorly
3*	F.	71	Right	—	12.10.43	Pneumococcus Type 8	40,000	30.11.43	7	5¼ oz.	Well and back to normal activity. No thickened pleura
4*	M.	63	Right	—	9.12.43	Haemolytic streptococcus	270,000	10.3.44	21	60 oz.	Well. Lung expanding but considerable pleural thickening. Pocket of 40 c.c. clear fluid—lymphocytes
5	F.	10	Left	Tuberculosis right apex. Right A.P.	11.12.43	Haemolytic streptococcus	155,000	4.2.44	10	20 oz.	Well. Still small pocket of fluid
6	F.	28	Right	Division of adhesions Haemorrhage—secondarily infected	6.1.44	Anaerobic non-haemolytic streptococcus	155,000	16.2.44	12	15 oz.	Afebrile. Dry. Haemoglobin 70%. Has had blood transfusion. Transferred to sanatorium
7	M.	52	Right	—	6.3.44	Pneumococcus Type 1	80,000	5.4.44	8	11½ oz.	Well. Some thickening

TABLE II.—STILL IN HOSPITAL.

No.	Sex	Age	Side	Complicating disease	Date of admission	Organism	Units of penicillin	No. of aspirations	Most removed at single aspiration	Present condition
8*	M.	10	Left	—	26.1.44	Pneumococcus Type 1	135,000	13	13 oz.	Afebrile for 6 weeks. Lung expanding but still small pocket
9	F.	31	Right	Very severe rheumatoid arthritis	1.3.44	Haemolytic streptococcus	100,000	10	5 oz.	Afebrile for 3 weeks. Still posterior pocket with thick wall
10	M.	49	Right	—	6.3.44	Pneumococcus Type 2	200,000	16	12 oz.	Developed anterior and posterior pocket. Anterior pocket now sterile and clear, posterior pocket still contains pneumococci
11	M.	41	Left	—	14.3.44	Pneumococcus Type 1	65,000	9	24 oz.	Became sterile after 65,000 but pneumococci reappeared. Now sterile and afebrile 2 weeks
12	M.	2	Left	Streptococcal pemphigus and bursitis over left elbow	14.3.44	Haemolytic streptococcus. Secondarily pneumococcus Type 10	65,000	Continuous neg. pressure drainage through needle for 5 days	18 oz.	Lung apparently re-expanded. Temperature subsided to below 100°F. Rapidly improving
13	M.	50	Right	—	22.3.44	Pneumococcus Type 24	45,000	5	15 oz.	Became sterile after 25,000 and developed bronchopleural fistula and became reinfected. Now sterile and afebrile 1 week
14	M.	21	Right	Traumatic haemothorax from bullet wound	4.4.44	Sterile	30,000	6	12 oz.	Well. Lung re-expanded

* Shown

B. Septicæmia

Cases by Members of the Staff of St. Mary's Hospital.

(1) Male, aged 30. History of **Bilateral Basal Pneumonia**—treated with sulphonamides—improved and relapsed. Did not improve with sulphonamides a second time. Staphylococci in blood. Metastatic prostatic abscess which burst into urethra.

(2) Male, aged 40. **Cavernous Sinus Thrombosis—Staphylococcal Septicæmia.** Multiple lung abscesses complicated by spontaneous pyopneumothorax and a retrobulbar abscess.

(3) Male. **Pneumonia with Streptococcal Septicæmia.**

(4) Male. **Carbuncle of Lip with Staphylococcal Pyæmia.**

Professor Alexander Fleming: In septicæmic cases penicillin must be administered systemically by intermittent injections, intravenous, intramuscular, or subcutaneous. The intramuscular route is probably the best; it is less painful than subcutaneous and it maintains the penicillin content of the blood rather longer than intravenous injection. After intramuscular injection of 15,000 units the penicillin content of the blood is at its height in about six minutes, so there is little time to be gained by intravenous injection. Penicillin can also be administered by a continuous drip, intravenous, intramuscular, or even subcutaneous. Intravenous drip has sometimes been complicated by phlebitis, and intramuscular drip is probably the method of choice, although if necessary the subcutaneous route can be employed. The dose for septicæmic cases is usually about 120,000 units in twenty-four hours—15,000 units (dissolved in 2 or 3 c.c. of normal saline) every three hours or by continuous drip—although Herrell of the Mayo Clinic has been successful with 60,000 units a day. Treatment is continued for from four to ten days according to the infecting organism, and the nature of the case. Blood samples are tested ten minutes after injection (intramuscular) to get the peak of the curve, and again after two or three hours to see how long the penicillin can be detected. After a dose of 15,000 units it has usually disappeared in three hours.

We have treated a considerable number of septicæmic cases, mainly staphylococcal but sometimes streptococcal or pneumococcal. Almost all of these were desperate cases which had not responded to sulphonamide treatment. None has died except one puerperal staphylococcal case which improved temporarily and then relapsed. Post-mortem showed extensive vegetations on the heart valves. One case shown had a staphylococcal septicæmia with cavernous sinus thrombosis and multiple lung abscesses with other complications. Such a case was not expected to live but after two courses of 1,200,000 units of penicillin (120,000 per day) he recovered completely.

Where there was a local focus as well as a general infection this was treated locally with penicillin at the same time that systemic treatment was given.

In severe carbuncles the systemic administration of 120,000 units for one or two days has prevented the spread of infection. Local treatment alone could then be pursued. This system is especially valuable in carbuncles of the face.

C. Osteomyelitis

Two Cases by RAINSFORD MOWLEM, F.R.C.S.

(1) **Massive Osteomyelitis of the Jaw.**

This patient has been shown as one of a series in which extensive resection of affected bone has been followed by complete closure of the wound and the local instillation of penicillin. This case was chosen as representing a partial failure, for a discharge persisted at the left angle of the jaw in spite of treatment. At the end of three weeks, although the pus was sterile, it became obvious that the surgery had been insufficiently radical. Further operation was undertaken and more diseased bone, which had obviously been previously overlooked, was removed. Subsequent recovery was uneventful.

From the series as a whole there has emerged the fact that penicillin alone cannot be expected to reverse the damage caused by bone defection, but that a combination of radical surgery and penicillin will enable these cases to be treated by the closed method, and thus to be healed by primary intention. It cannot be too often stressed that the presence of dead bone is an indication for surgery, and not for penicillin.

(2) (Shown by Squadron Leader A. B. MACGREGOR). Patient, female. **Actinomycosis of the Right Side of Mandible.**

This case of well-established actinomycosis is shown to illustrate the fact that there may be more than one subgroup of the causal streptothrix. In spite of reports from

other hospitals that no result had been obtained in the treatment of this condition with penicillin, cultures from this patient were tested for sensitivity. Cultures obtained from other patients suffering from actinomycosis had been shown to be completely insensitive, but in this case the sensitivity was found to be between two and four times greater than that obtained with the standard Oxford staphylococcus. Local treatment was therefore undertaken with extremely satisfactory results, and it may be that sensitivity to penicillin is a means of differentiating the streptothrix group.

Male, aged 8. Osteomyelitis with Pyæmia.—M. E. FLOREY, M.B. Treated by penicillin for one month.

That the temperature curve is not necessarily a good guide to progress in the early stages of treatment was demonstrated in this case of staphylococcal pyæmia with multiple foci in bones, joints and lungs. Though complete recovery was evidenced by the elimination of staphylococci from every available lesion and non-recurrence of the condition over a period of eighteen months, a swinging temperature curve accompanied the first nine days of treatment. It only reached normal levels three weeks after the first administration of penicillin.

Lt.-Colonel C. F. Koch (Consulting Surgeon to Netherlands Army) described the techniques used in different hospitals in America. In the Mayo clinic a continuous intravenous drip was used, with a daily dosage of not more than 40,000 to 60,000 units. At a New York hospital Dr. Chang Lyons combined the intramuscular treatment with local application to the wounds with excellent results in cases of chronic osteomyelitis after compound fractures.

Two Cases shown by D. RANGER, F.R.C.S, for R. VAUGHAN HUDSON, F.R.C.S.

(1) D. S., male, aged 7. Staphylococcal Septicæmia and Meningism, due to Acute Osteomyelitis of the Right Tibia, treated by penicillin and aspiration of circumosseous abscess. Five months later subacute tissue abscess formed.

(2) L. H., male, aged 8. Admitted 23.8.42. Staphylococcal Septicæmia and Meningism due to Acute Osteomyelitis of the Lower End of the Femur, treated by sulphathiazole and surgery. Persistent staphylococcal sinus for thirteen months; eventual subacute infective arthritis.

CASE I.—Surgery avoided, no residual sinuses. Healing and rehabilitation occurring in one-third of the time. The recurrence five months later responded rapidly to a second course of penicillin and aspiration.

CASE II.—Systemic penicillin healed the sinus and restored to normal the function of the joint.

Freedom from recurrence cannot be guaranteed in either case.

Three patients Treated with Crude Penicillium Filtrate shown by J. M. ALSTON, M.R.C.P., and E. T. BAILEY, F.R.C.S., from Fracture "A" Dept., Northern Hospital, N.21.

(1) H. W., male, aged 28. Chronic Osteomyelitis of Sacrum. Multiple Sinuses.
(2) R. W., male, aged 25. Compound Fracture of Right Femur and Shell Wound.
(3) F. P., male, aged 17. Staphylococcal Osteomyelitis of Tibia and Abscess of Thigh.

Dr. J. M. Alston : The main interest of the three patients shown by Mr. Bailey and me is that they are examples of subacute or chronic suppuration of bone or soft tissues treated by crude penicillium filtrate. The results, we think, bear comparison with those with the calcium salt of penicillin in similar cases although our patients received only 800, 1,000 and 1,500 Oxford units respectively. As well as these three, 18 other patients have been treated by different surgeons with similar filtrates, containing 4 to 8 units per c.c., made in my laboratory. In 17 of the total 21, the surgeon believed that the treatment was successful, often to an astonishing degree, and in 4, success was absent or doubtful. The features in the successful cases were decrease of suppuration, increase of granulation tissue and of epithelialization, healing and very quick reduction of general toxæmia. The diagnoses of the 18 additional patients were subacute or chronic osteomyelitis and infection of soft tissues, unhealed accidental wounds, chronic syphilitic ulceration, chronic X-ray burn, vulvo-vaginitis, breast abscess. In most of these patients, sulphonamide treatment had failed.

Female, aged 23. Burns from Paint-spray Fire.—A. J. HOBSON, F.R.C.S.

1st and 2nd degree on face and hands and 3rd on right forearm.
Crude penicillin dressings applied to burns rapidly become adherent and peel off in about seven to ten days leaving a well-healed surface. All cases treated so far have been equally successful and have been free from pain, sepsis or shock. The medium now

B. Septicæmia

Cases by Members of the Staff of St. Mary's Hospital.

(1) Male, aged 30. History of Bilateral Basal Pneumonia—treated with sulphonamides—improved and relapsed. Did not improve with sulphonamides a second time. Staphylococci in blood.

(2) Male, aged 40. Cavernous Sinus Thrombosis—Staphylococcal Septicæmia. Multiple lung abscesses complicated by spontaneous pyopneumothorax and a retrobulbar abscess. Metastatic prostatic abscess which burst into urethra.

(3) Male. Pneumonia with Streptococcal Septicæmia.

(4) Male. Carbuncle of Lip with Staphylococcal Pyæmia.

Professor Alexander Fleming: In septicæmic cases penicillin must be administered systemically by intermittent injections, intravenous, intramuscular, or subcutaneous. The intramuscular route is probably the best; it is less painful than subcutaneous and it maintains the penicillin content of the blood rather longer than intravenous injection. After intramuscular injection of 15,000 units the penicillin content of the blood is at its height in about six minutes, so there is little time to be gained by intravenous injection. Penicillin can also be administered by a continuous drip, intravenous, intramuscular, or even subcutaneous. Intravenous drip has sometimes been complicated by phlebitis, and intramuscular drip is probably the method of choice, although if necessary the subcutaneous route can be employed. The dose for septicæmic cases is usually about 120,000 units in twenty-four hours—15,000 units (dissolved in 2 or 3 c.c. of normal saline) every three hours or by continuous drip—although Herrell of the Mayo Clinic has been successful with 60,000 units a day. Treatment is continued for from four to ten days according to the infecting organism, and the nature of the case. Blood samples are tested ten minutes after injection (intramuscular) to get the peak of the curve, and again after two or three hours to see how long the penicillin can be detected. After a dose of 15,000 units it has usually disappeared in three hours.

We have treated a considerable number of septicæmic cases, mainly staphylococcal but sometimes streptococcal or pneumococcal. Almost all of these were desperate cases which had not responded to sulphonamide treatment. None has died except one puerperal staphylococcal case which improved temporarily and then relapsed. Post-mortem showed extensive vegetations on the heart valves. One case shown had a staphylococcal septicæmia with cavernous sinus thrombosis and multiple lung abscesses with other complications. Such a case was not expected to live but after two courses of 1,200,000 units of penicillin (120,000 per day) he recovered completely.

Where there was a local focus as well as a general infection this was treated locally with penicillin at the same time that systemic treatment was given.

In severe carbuncles the systemic administration of 120,000 units for one or two days has prevented the spread of infection. Local treatment alone could then be pursued. This system is especially valuable in carbuncles of the face.

C. Osteomyelitis

Two Cases by Rainsford Mowlem, F.R.C.S.

(1) Massive Osteomyelitis of the Jaw.

This patient has been shown as one of a series in which extensive resection of affected bone has been followed by complete closure of the wound and the local instillation of penicillin. This case was chosen as representing a partial failure, for a discharge persisted at the left angle of the jaw in spite of treatment. At the end of three weeks, although the pus was sterile, it became obvious that the surgery had been insufficiently radical. Further operation was undertaken and more diseased bone, which had obviously been previously overlooked, was removed. Subsequent recovery was uneventful.

From the series as a whole there has emerged the fact that penicillin alone cannot be expected to reverse the damage caused by bone defection, but that a combination of radical surgery and penicillin will enable these cases to be treated by the closed method, and thus to be healed by primary intention. It cannot be too often stressed that the presence of dead bone is an indication for surgery, and not for penicillin.

(2) (Shown by Squadron Leader A. B. MacGregor). Patient, female. Actinomycosis of the Right Side of Mandible.

This case of well-established actinomycosis is shown to illustrate the fact that there may be more than one subgroup of the causal streptothrix. In spite of reports from

zing (ureteric catheter) the tendon sheath through the punctured wound, enlarging if necessary, washing out the pus or infected synovial fluid with saline and then instilling one or two c.c. of a strong penicillin fluid. This instillation was repeated each day for seven days and the catheter removed. Movements were now started, and full function was quickly restored, a result never to be achieved in pre-penicillin days. It was noticed in doing these cases that very high pressures prevailed in the tendon sheath although it was freely open at the site of the wound and quite viscid fluid would exude under obvious pressure from the fine ureteric catheter immediately it was introduced. The X-ray (*see* fig.) shows the catheter in position.

Female, aged 24, machinist. Acute Tendon Sheath Infection.—M. E. FLOREY, M.B.
Treated 29.1.43 to 13.2.43.
Duration of complaint five days. Infecting organism *Staph. aureus.*
Findings at operation.—Purulent sinus leading into sheath which contained excess turbid fluid.
Treatment.—Lateral digital and palmar incisions into sheath. Wounds packed with penicillin powder and paste 1,000 units/g. decreasing later.
Result.—Healed in seventeen days. Full function and return to work within six weeks without physiotherapy or special exercises.

Dr. M. E. Florey : Reduction in healing time and full functional recovery without the necessity of special therapy can be expected in acute tendon sheath infections, provided they are treated, in conjunction with surgery, in the earliest stages of infection—before the fluid has become frankly purulent.

E. Meningitis

Male, aged 47 (St. Mary's Hospital).
Two months' history of meningeal symptoms previous to admission. Investigated thoroughly and nothing obtained bacteriologically, in spite of pyrexia up to 103°, until 14 days prior to admission, when *Streptococcus viridans* was found. He had been given several courses of sulphonamides without result.

Mr. A. Dickson Wright : In a series of six cases at St. Mary's Hospital there have been two deaths in each case from pus loculations over the convexities of the hemispheres. In the last two cases this space has been filled with penicillin by the following manœuvre. The ventricles were tapped till they were dry and the cortex was noticed to shrink away from the dura, and a fine rubber catheter was passed into this space over the convexities and penicillin run in and agitated by forced respirations and straining on the part of the patient. This rubber tube might be left for a few days in a bad case.

F. Ulcerative Blepharitis

Male, aged 32, bus conductor. Chronic Ulcerative Blepharitis.—M. E. FLOREY, M.B.
Treated 24.2.42 to 6.5.42.
Duration of complaint thirty-two years. Infecting organism *Staph. aureus.*
Full recovery without relapses from chronic ulcerative blepharitis can be expected provided the treatment is carried out for long enough. In the case demonstrated this time was eight weeks—the indication for cessation of treatment not being the disappearance of symptoms but the elimination of staphylococci from the lids after treatment had been discontinued for several days.

G. Anaerobic Streptococcal Septicæmia

Puerperal Anaerobic Streptococcal Septicæmia: Three Cases Treated with Penicillin.—A. DOLPHIN, M.D. (introduced by R. CRUICKSHANK, M.D.).

Puerperal anaerobic streptococcal septicæmia occurs most commonly after abortion or after prolonged and difficult full-term delivery; retained products seem to favour its development. Pathologically it begins as a uterine infection with septic thrombophlebitis of the pelvic veins, followed by multiple metastatic lung abscesses and sometimes by empyema. Cases may occur with a rapid onset and a fulminating course; more commonly some days elapse after abortion before any evidence of illness appears. Often the first symptom is a rigor and the full syndrome shows itself by frequent rigors, swinging temperature, signs of lung involvement and a fatality rate of 80 to 90%. A simila

used is free from all organic substance except saccharose. A filtrate is obtained by either porcelain filtration (which appears to lower the titre somewhat) or by the use of filter paper. It is hoped that this filtrate, free from the production of further metabolites, will prove reasonably stable and even concentratable. If so it will enable pure penicillin to be reserved for intravenous and intramuscular use. The strength of crude dressings, although much below that used with pure penicillin, appears to be adequate for bacteriostasis. One interesting observation is that *B. pyocyaneus* appears in quite a large number of cases when other organisms have been eliminated with penicillin. A little weak acetic acid, however, rapidly clears it away.

D. Tendon Sheath Infection

Two Cases of Tendon Sheath Infection. (Shown by Staff of St. Mary's Hospital.)

(1) **Puncture Wound of Tendon Sheath—Staphylococcal Teno-synovitis.**

A factory worker pricked his finger with a sliver of wood. The finger became swollen, red and tender, and movements were very painful. On examination the tendon sheath was obviously infected, and there was a small septic wound over the terminal phalangeal joint. The wound was slightly enlarged and a ureteric catheter passed up the sheath. The pus and synovial fluid were washed out and 1 c.c. penicillin instilled every day for eight days. Temperature and all symptoms vanished and a good functioning finger was obtained. (Cultures—*Staph. aureus*.)

(2) Housewife: Puncture wound with a sewing needle led to a Suppurative Teno-synovitis with mixed organisms in the pus. Instillations with penicillin 1 c.c. daily led to complete healing and good function.

Mr. A. Dickson Wright: In early tendon sheath infections generally due to punctured wounds of the sheath itself penicillin offers the only chance of a functioning tendon such as was obtained in both the cases shown to-day. The technique consists in catheteri-

The catheter is shown in antero-posterior and lateral views traversing the wound in the front of the finger and passing the whole length of the tendon sheath.

zing (ureteric catheter) the tendon sheath through the punctured wound, enlarging if necessary, washing out the pus or infected synovial fluid with saline and then instilling one or two c.c. of a strong penicillin fluid. This instillation was repeated each day for seven days and the catheter removed. Movements were now started, and full function was quickly restored, a result never to be achieved in pre-penicillin days. It was noticed in doing these cases that very high pressures prevailed in the tendon sheath although it was freely open at the site of the wound and quite viscid fluid would exude under obvious pressure from the fine ureteric catheter immediately it was introduced. The X-ray (*see* fig.) shows the catheter in position.

Female, aged 24, machinist. **Acute Tendon Sheath Infection.**—M. E. FLOREY, M.B.
Treated 29.1.43 to 13.2.43.
Duration of complaint five days. Infecting organism *Staph. aureus.*
Findings at operation.—Purulent sinus leading into sheath which contained excess turbid fluid.
Treatment.—Lateral digital and palmar incisions into sheath. Wounds packed with penicillin powder and paste 1,000 units/g. decreasing later.
Result.—Healed in seventeen days. Full function and return to work within six weeks without physiotherapy or special exercises.

Dr. M. E. Florey: Reduction in healing time and full functional recovery without the necessity of special therapy can be expected in acute tendon sheath infections, provided they are treated, in conjunction with surgery, in the earliest stages of infection—before the fluid has become frankly purulent.

E. Meningitis

Male, aged 47 (St. Mary's Hospital).
Two months' history of meningeal symptoms previous to admission. Investigated thoroughly and nothing obtained bacteriologically, in spite of pyrexia up to 103°, until 14 days prior to admission, when *Streptococcus viridans* was found. He had been given several courses of sulphonamides without result.

Mr. A. Dickson Wright: In a series of six cases at St. Mary's Hospital there have been two deaths in each case from pus loculations over the convexities of the hemispheres. In the last two cases this space has been filled with penicillin by the following man-œuvre. The ventricles were tapped till they were dry and the cortex was noticed to shrink away from the dura, and a fine rubber catheter was passed into this space over the convexities and penicillin run in and agitated by forced respirations and straining on the part of the patient. This rubber tube might be left for a few days in a bad case.

F. Ulcerative Blepharitis

Male, aged 32, bus conductor. **Chronic Ulcerative Blepharitis.**—M. E. FLOREY, M.B.
Treated 24.2.42 to 6.5.42.
Duration of complaint thirty-two years. Infecting organism *Staph. aureus.*
Full recovery without relapses from chronic ulcerative blepharitis can be expected provided the treatment is carried out for long enough. In the case demonstrated this time was eight weeks—the indication for cessation of treatment not being the disappearance of symptoms but the elimination of staphylococci from the lids after treatment had been discontinued for several days.

G. Anaerobic Streptococcal Septicæmia

Puerperal Anaerobic Streptococcal Septicæmia: Three Cases Treated with Penicillin.—
A. DOLPHIN, M.D. (introduced by R. CRUICKSHANK, M.D.).

Puerperal anaerobic streptococcal septicæmia occurs most commonly after abortion or after prolonged and difficult full-term delivery; retained products seem to favour its development. Pathologically it begins as a uterine infection with septic thrombophlebitis of the pelvic veins, followed by multiple metastatic lung abscesses and sometimes by empyema. Cases may occur with a rapid onset and a fulminating course; more commonly some days elapse after abortion before any evidence of illness appears. The first symptom is a rigor and the full syndrome shows itself by frequent rigors, swinging temperature, signs of lung involvement and a fatality rate of 80 to 90%. A similar

used is free from all organic substance except saccharose. A filtrate is obtained by either porcelain filtration (which appears to lower the titre somewhat) or by the use of filter paper. It is hoped that this filtrate, free from the production of further metabolites, will prove reasonably stable and even concentratable. If so it will enable pure penicillin to be reserved for intravenous and intramuscular use. The strength of crude dressings, although much below that used with pure penicillin, appears to be adequate for bacteriostasis. One interesting observation is that *B. pyocyaneus* appears in quite a large number of cases when other organisms have been eliminated with penicillin. A little weak acetic acid, however, rapidly clears it away.

D. Tendon Sheath Infection

Two Cases of Tendon Sheath Infection. (Shown by Staff of St. Mary's Hospital.)

(1) **Puncture Wound of Tendon Sheath—Staphylococcal Teno-synovitis.**

A factory worker pricked his finger with a sliver of wood. The finger became swollen, red and tender, and movements were very painful. On examination the tendon sheath was obviously infected, and there was a small septic wound over the terminal phalangeal joint. The wound was slightly enlarged and a ureteric catheter passed up the sheath. The pus and synovial fluid were washed out and 1 c.c. penicillin instilled every day for eight days. Temperature and all symptoms vanished and a good functioning finger was obtained. (Cultures—*Staph. aureus.*)

(2) Housewife: Puncture wound with a sewing needle led to a **Suppurative' Teno-synovitis** with mixed organisms in the pus. Instillations with penicillin 1 c.c. daily led to complete healing and good function.

Mr. A. Dickson Wright: In early tendon sheath infections generally due to punctured wounds of the sheath itself penicillin offers the only chance of a functioning tendon such as was obtained in both the cases shown to-day. The technique consists in catheteri-

The catheter is shown in antero-posterior and lateral views traversing the wound in the front of the finger and passing the whole length of the tendon sheath.

zing (ureteric catheter) the tendon sheath through the punctured wound, enlarging if necessary, washing out the pus or infected synovial fluid with saline and then instilling one or two c.c. of a strong penicillin fluid. This instillation was repeated each day for seven days and the catheter removed. Movements were now started, and full function was quickly restored, a result never to be achieved in pre-penicillin days. It was noticed in doing these cases that very high pressures prevailed in the tendon sheath although it was freely open at the site of the wound and quite viscid fluid would exude under obvious pressure from the fine ureteric catheter immediately it was introduced. The X-ray (*see* fig.) shows the catheter in position.

Female, aged 24, machinist. **Acute Tendon Sheath Infection.**—M. E. FLOREY, M.B.
Treated 29.1.43 to 13.2.43.
Duration of complaint five days. Infecting organism *Staph. aureus.*
Findings at operation.—Purulent sinus leading into sheath which contained excess turbid fluid.
Treatment.—Lateral digital and palmar incisions into sheath. Wounds packed with penicillin powder and paste 1,000 units/g. decreasing later.
Result.—Healed in seventeen days. Full function and return to work within six weeks without physiotherapy or special exercises.

Dr. M. E. Florey : Reduction in healing time and full functional recovery without the necessity of special therapy can be expected in acute tendon sheath infections, provided they are treated, in conjunction with surgery, in the earliest stages of infection—before the fluid has become frankly purulent.

E. Meningitis

Male, aged 47 (St. Mary's Hospital).
Two months' history of meningeal symptoms previous to admission. Investigated thoroughly and nothing obtained bacteriologically, in spite of pyrexia up to 103°, until 14 days prior to admission, when *Streptococcus viridans* was found. He had been given several courses of sulphonamides without result.

Mr. A. Dickson Wright : In a series of six cases at St. Mary's Hospital there have been two deaths in each case from pus loculations over the convexities of the hemispheres. In the last two cases this space has been filled with penicillin by the following manœuvre. The ventricles were tapped till they were dry and the cortex was noticed to shrink away from the dura, and a fine rubber catheter was passed into this space over the convexities and penicillin run in and agitated by forced respirations and straining on the part of the patient. This rubber tube might be left for a few days in a bad case.

F. Ulcerative Blepharitis

Male, aged 32, bus conductor. **Chronic Ulcerative Blepharitis.**—M. E. FLOREY, M.B.
Treated 24.2.42 to 6.5.42.
Duration of complaint thirty-two years. Infecting organism *Staph. aureus.*
Full recovery without relapses from chronic ulcerative blepharitis can be expected provided the treatment is carried out for long enough. In the case demonstrated this time was eight weeks—the indication for cessation of treatment not being the disappearance of symptoms but the elimination of staphylococci from the lids after treatment had been discontinued for several days.

G. Anaerobic Streptococcal Septicæmia

Puerperal Anaerobic Streptococcal Septicæmia : Three Cases Treated with Penicillin.—
A. DOLPHIN, M.D. (introduced by R. CRUICKSHANK, M.D.).
Puerperal anaerobic streptococcal septicæmia occurs most commonly after abortion or after prolonged and difficult full-term delivery; retained products seem to favour its development. Pathologically it begins as a uterine infection with septic thrombophlebitis of the pelvic veins, followed by multiple metastatic lung abscesses and sometimes by empyema. Cases may occur with a rapid onset and a fulminating course; more commonly some days elapse after abortion before any evidence of illness appears. Often the first symptom is a rigor and the full syndrome shows itself by frequent rigors, swinging temperature, signs of lung involvement and a fatality rate of 80 to 90%. A similar

syndrome has been described in connexion with peritonsillar infections and in these a septic thrombophlebitis of the peritonsillar veins with spread to the internal jugular occurs associated with metastatic lung abscesses. The infection is also caused by *Bact. necrophorum* (or *B. funduliformis*) but the anaerobic streptococcus is the more common pathogen.

The anaerobic streptococcus grows slowly in culture. This delay and the arrival of some patients in hospital after they had been ill for many days (and in one case four weeks) may make it impossible to begin penicillin treatment at the time most favourable for cure, i.e. before lung complications have established themselves. Three cases of the puerperal infection have been treated at the Puerperal Sepsis Unit of the L.C.C., North-Western Hospital, during 1943.

CASE I (aged 27).—Abortion 12.8.43. Admitted 13.8.43. Fulminating infection with pelvic peritonitis and thrombophlebitis, swinging temperature, numerous rigors and extreme toxæmia. M & B 693, 41 g., by continuous drip, with no response.
Blood cultures on August 21 and 25 grew the anaerobic streptococcus and *B. coli*.
Penicillin started on 25.8.43; total dosage 510,000 units by intravenous drip during six days. Blood culture negative to the anaerobic streptococcus but positive to *B. coli* on August 27 and 30. There was a definite improvement after penicillin, but toxæmia remained extreme, bronchopneumonia appeared and death occurred on 31.8.43. At autopsy there were multiple septic lung infarcts, septic thrombus in the right internal iliac vein, a pelvic abscess and necrosis of the fundus uteri.

CASE II (aged 36).—Abortion 5.8.43. Admitted to the Puerperal Sepsis Unit on 12.8.43. Uterine sepsis and general peritonitis. The acute peritonitis subsided, but despite M & B 693, 51 g., the general condition deteriorated and maniacal delirium developed.
Blood cultures on August 17, 19, 20, 22 and 25, 1943, grew an anaerobic streptococcus. Penicillin was started on 25.8.43 and continued for sixteen days (total dosage 1,680,000 units by intramuscular injections of 15,000 units three-hourly) and blood cultures were sterile on August 27 and 30. In three days the general condition had immensely improved and from being maniacally delirious the patient became completely rational. Progress was maintained until 9.9.43 when she developed intestinal obstruction due to multiple adhesions and died despite operation.
At autopsy there were multiple septic lung infarcts, multiple, dense peritoneal adhesions, and partial necrosis of the uterus. On admission to hospital the patient's blood and cerebrospinal fluid gave a strongly positive Wassermann reaction, but after penicillin the blood W.R. became practically negative, whereas the cerebrospinal fluid W.R. remained strongly positive. At no time was penicillin found in the cerebrospinal fluid.

CASE III (aged 32).—Forceps delivery on 2.10.43. Pyrexia and rigors since 5.10.43. Admitted to North-Western Hospital on 1.11.43; toxic, numerous rigors, swinging temperature, and dyspnœa due to asthma, bronchopneumonia and myocarditis. Blood cultures grew an anaerobic streptococcus on 22.10.43, 2.11.43 and 3.11.43. Penicillin started on 3.11.43, i.e. four weeks after onset of symptoms; blood cultures were negative on November 5, 8 and 11. Penicillin was stopped after three days (total dosage: 345,000 units by intramuscular injections of 15,000 units three-hourly) because, despite the negative blood cultures, the general condition was not improved, and severe bronchopneumonia and toxæmia were still present. Death occurred on 18.11.43.
At autopsy there were multiple lung abscesses but the pelvic veins were clear of infection.

Dr. R. Cruickshank: Anaerobic streptococcus septicæmia with its septic thrombophlebitis and metastatic abscesses is somewhat akin to generalized staphylococcal infection, and is equally resistant to sulphonamide therapy, presumably because the drug cannot penetrate into septic blood clot. The diffusibility of penicillin and the dramatic response in staphylococcal pyæmia prompted us to try this drug in cases of anaerobic streptococcal septicæmia admitted to the Puerperal Sepsis Unit of the North-Western Hospital (L.C.C.). While the results have so far been disappointing, they do not negative further trial, and the absence of septic thrombus in the last case (a unique finding, in my experience) indicates that penicillin can cure the primary focus. The syndrome is unfamiliar to most clinicians and may occur after infected war wounds as well as septic abortion, peritonsillar abscess and appendicitis. Early diagnosis is essential if penicillin-therapy is to have a fair trial. Anaerobic blood culture needs to be practised more commonly in pyrexias of unknown origin, and the nature of the infecting organism in this syndrome must be determined before penicillin is given, for while all strains of anaerobic streptococcus so far tested have been penicillin-sensitive, two out of three necrophorus strains were resistant. As regards generalized staphylococcal infection, I should like to urge the necessity of *quantitative* blood culture for accurate prognosis in this type of infection.

Section of the History of Medicine

President—Sir WALTER LANGDON-BROWN, M.D.

[*December* 1, 1943]

The " Breviary " and " Dyetary " of Andrew Boorde (1490-1549), Physician, Priest and Traveller [*Synopsis*]

By DOUGLAS GUTHRIE, M.D.

THE name of Andrew Boorde is seldom mentioned by historians of medicine. When noted at all, he is sometimes passed off as a mere buffoon or mountebank, the original "Merry Andrew". The sources of information on his life and work are scanty; nevertheless, to anyone who cares to collect and arrange the available evidence, Andrew Boorde will become an important figure of Tudor times. Like the character, so familiar in fiction, in history, or in current life, who is constantly assumed to be a fool, while all the time he is really fooling his critics, Boorde becomes steadily wiser the closer we inspect him.

As author of the first book on Medicine originally written in the English language, *The Breviary of Health,* and of the first guide-book to the Continent, *The First Boke of the Introduction of Knowledge,* he surely deserves our attention. His other important works, very popular in their day, were *The Dyetary of Health,* a companion volume to the *Breviary; The Pryncyples of Astronomye;* and *The Itinerary of England,* usually called *The Perigrination of Doctor Boarde.*

THE LIFE AND TRAVELS OF ANDREW BOORDE

Andrew Boorde was born about 1490 at Boord's Hill, near Cuckfield, in Sussex. His name is sometimes written Borde or Boarde, and the fact that he called himself Andreas Perforatus suggests that it was pronounced "bored". As an Oxford graduate his name appears in Wood's *Athenae Oxoniensis.* His career as a Carthusian monk was not long; within a few years he found himself "nott able to byde the rigourosite of your religion". Thus, he wrote to his Superior. This petition being granted, he went abroad to study medicine at Montpellier, "the nobilist universite of the world for physicions and surgions". On his return he was recognized in Court circles, but the desire to see more of the world was strong, and he departed on a pilgrimage to Saint James of Compostel (Santiago) in Spain, along with nine English and Scottish pilgrims with whom he forgathered at Orleans. Boorde tells us that he was the sole survivor of this expedition, and that he "would rather go five times to Rome than once to Compostel". The account of his next, the third, continental journey is partly given in his letters to Secretary Thomas Cromwell, for whom he acted as an emissary or ambassador in order to ascertain the attitude towards King Henry VIII, which he found far from favourable. Next, we find Boorde in Scotland, where he spent a year "in a lityl universite namyd Glasco", where he studied and "did practyce physik for the sustentacion of my lyving".

It was during the fourth and final tour of the Continent that he completed, at Mont-

pellier, his *First Boke of the Introduction of Knowledge,* which may fairly claim to be the first guide-book to the Continent to be written in English and printed in England.

Eventually, Andrew Boorde settled in practice at Winchester, where he was esteemed as "a noted poet, a witty and ingenious person, and an excellent physician". Trouble clouded his later years, when he was accused, with what degree of justice we know not, of keeping at Winchester three women of questionable morals. At all events, he found himself imprisoned in the Fleet in London, and there he died in 1549. Further details of his life and journeys may be found in the attractive edition of the *Introduction* and the *Dyetary* which was edited in 1870 for the English Text Society by F. J. Furnivall.

THE "BREVIARY OF HEALTH"

From the medical point of view, Andrew Boorde's most important work is his *Breviary of Health,* 1547, a sort of handbook of domestic medicine after the fashion of the *Regimen of Salerno.* Although, as already mentioned, it was the first medical book, by a medical man, originally written and printed in the English language, it was not the first effort of its kind.

In 1534 Sir Thomas Elyot had published his *Castel of Health,* and had incurred the wrath of physicians for doing so.

Boorde, anxious to avoid all semblance of self-advertisement or quackery, prefaces his *Breviary* by five lengthy explanations of his reason for writing it. Consideration of space forbids us to print more than a brief quotation from the first preface. It is "A Prologue to Physitions", and Boorde addresses them thus: "Egregious doctours and maisters of the Eximious and Archane Science of physick, of your Urbanitie exasperate not yourselves against mee, for making of this little volume of physicke, considering that my pretence is for an utilitie and a common wealth." He proceeds, at considerable length, to discuss the need for a sound medical education, and to enumerate the arts and sciences necessary to the physician. He must have Grammar to understand what he doth read, Logic to discuss and define truth from falsehood, Geometry to weigh and measure his drugs and potions, and an eloquent tongue to convince his patients. "He that hath not the aforesaid sciences, shall kill many more than he shall save."

The Breviary of Health consists of 384 short chapters, with an appendix called "The Second Booke, named the *Extravagantes*", of 73 chapters. The material is arranged alphabetically from A to Z, from "Abstinence to Zirbus". Abstinence is "the most perfectest medicine that can bee, after repletion or surfet". Zirbus (the omentum) is "a pannicle or caule that doth cover the guts: it doth keep the heate of them and doth defend the cold". Of subjects there is an infinite variety; Black Melancholy, Kings Evill, Dulness of Wit, Sleep, Memory, Megrim, Warts, Fleas, Pestilence, to mention a few at random. "Musicke" is defined as "one of the liberal sciences comfortable to man in sickness and in health". Gonorrhœa "is named so because Gomorra and Sodom did sinke for such like matter".

Some curious remedies are mentioned. For "Defnes", we are to "take the gall of a hare and mix it with the grece of a Fox and with black woll instill it into the ears"; for "Dronkennes", "drink in the morning a dish of milk"; for "Squint or Goggle eye", "put nothing into the eye but the blood of a dove". To counteract fear, "use mery company and feare nothing but God". Some of the treatment is more heroic. The cure of Itching is to "prepare a good payre of nayles, to scratch and claw and tear and rend the skin, that the corrupt blood may run out". There is an equally drastic treatment of Quinsy; it is worth quoting in full: "The 21 Chapter doth shew of the Squincy. Angina is the Latin word, Sinachi the Greek word. It is an impostum in the throat which doth stop up a man's wind or breath, and doth come of rheume descending from the head or vaporous humours ascending from the stomacke. A Remedy: Take a little piece of Pork or Bacon and tie about it a strong thread and let the patient swallow it and by and by pull it out again. Be sure to hold fast the thred and pull it out quickly."

In another chapter we learn that sleeplessness comes of "studying or musyng too much on some matter in the which some persons doth wade too farre, bringing themselves into fantasies". The remedy is leaves of lettuce laid on the temples.

No less than twenty kinds of fevers are described, with curious names, erratic fever, tetrach fever, and putrefied fever, besides the more familiar quartan and tertian. The second book of the *Breviary,* or *Extravagantes,* contains several chapters on examination of the urine, or water casting, as it was called. Boorde wisely remarks that "the best doctour of Physicke may bee deceived in an urine".

DIETETICS IN THE SIXTEENTH CENTURY

Probably the most interesting and the best-written of Andrew Boorde's works is the companion volume to the *Breviary* which he called the *Compendyous Regyment* or *Dyetary of Health*. It contains much sound advice which might apply even to-day. Commencing with directions on the choosing of a site for one's house, where there is plenty of wood and water and "elbow-rome", as well as abundance of fresh air, he notes that there must be no stinking ponds, nor corrupt dunghills in the vicinity. 'As dust doth putrefy the ayre, the swepynge of howses ought nat to be done as long as any honest man is within the precynct.'

Then follows a chapter on the care of soul and body. The head of the house must always punish swearers, "for in all the world there is not such odious swearing as is used in Englande, especially among youth and children". Seven hours sleep is enough for most men, and healthy men should not sleep by day, but if they must do so, let them "leayne and slepe agunst a cupborde, or else syttyng upryght in a chayre". There should be a fire in one's bedroom to purify the air and consume evil vapours, and the windows should be kept closed at night. "Slepe on your ryght syde . . . with your heed hygh; have a good thycke quylt . . . and let your nyght-cap be of skarlet. When you ryse in the morning, ryse with myrth and remember God." After eight chapters of such counsel, we come to the main subject of the work, a discussion of diet, first, that for a healthy man, and then the diet advised for the sick. Repletion shortens a man's life, we are told, and two meals a day should suffice, except for a labourer, who may require three. Water should never be drunk by itself, but may be used to dilute wine. Rain water is best, next comes running water, and lastly, well water. Standing water engenders illness. Ale is the natural drink for an Englishman. As for bread, this should be of pure wheat, and not of mixed grains. Despite his dislike of Scotland, the author regards oatcake as "a lordly dish".

Milk is good for old men, melancholy men, children, and consumptives. Sea fish are more wholesome than river fish, which may taste of mud, and fish and flesh should not be eaten at the same meal.

There seems to have been great variety of game in Boorde's day. A bustard is nutritious meat, and a bittern is not so hard to digest as a heron. Plovers and lapwings are not so nourishing as turtle-doves. Of small birds, the lark is best; thrushes are also good, but "not titmouses or wrens, because they eat spiders".

The latter half of the *Dyetary* is devoted to the place of diet in sickness. "A good coke is halfe a physicyon. The chief physick doth come from the kytchen wherefore the physician and the coke for sycke men must consult togyther." It is interesting to note that the sufferer from asthma should avoid nuts, cheese, milk and fish, and should beware of dust and smoke.

Lunatics should have hot meals three times a day, but no wine or strong ale. Their heads should be shaven once a month, and they should be kept in a close dark room with a keeper whom they fear.

Boorde pursues his subject to the end, for his last chapter deals with the proper ordering of a death bed, which should have good nurses, sweet odours, and no babbling women.

Anyone who cares to read the *Dyetary of Health* will be convinced that Andrew Boorde was a shrewd and sensible physician, and that, although his anatomy was not always accurate and his pathology was of the humoral variety, in many other respects he held views far in advance of his time.

He was a happy and good-natured man who appears to have taken as his motto his oft-quoted remark that "Myrth is one of the chiefest thynges in Physicke", and who surely deserves to hold a more honoured place in the history of medicine than has hitherto been accorded to him.

BIBLIOGRAPHY

AIKIN, JOHN (1813) Biographical Notices of the Medical Profession. London.
COLWELL, H. A. (1911) Andrew Boorde and his medical works. *Middlesex Hosp. Journ.*, 15, 25.
FOX, ARTHUR W. (1899) A Book of Bachelors. London.
FULLER, THOMAS (1811) The History of the Worthies of England. New Edit. London.
FURNIVALL, F. J. (1870) Edited. Andrew Boorde's "Introduction of Knowledge" and "Dyetary of Health."
   Early English Text Society.
POOLE, H. E. (1936) The Wisdom of Andrew Boorde. Leicester.
SCARLETT, E. P. (1937) A Tudor Worthy: Master Andrew Boorde of Physicke Doctour. *Canad. Med. Assoc.*
   Journ., 38, 588.
WOOD, ANTHONY (1813) Athenae Oxoniensis.

Health and Sickness in the Merchant Navy to 1815 [*Abstract*]

By J. A. Nixon, C.M.G., M.D.

PRINCE HENRY the Navigator, third son of King John I of Portugal and nephew of King Henry IV of England, was the originator of all modern merchant navies. In 1415 he founded at Sagres, near Cape St. Vincent, a Naval College or Maritime University. He brought there the world's best navigators and shipbuilders. Travellers and merchants were encouraged to bring trade gossip from every quarter. Old pilots contributed their experience and the charts they had made. Ship masters came there to learn how to use instruments like the compass and astrolabe, or how to read maps. Jews and Arabians were sent for on account of their knowledge of mathematics and astronomy. Henry remained at Sagres for forty-five years and began to see his labours bear fruit. The age of ocean travel and discovery opened. Madeira was discovered in 1419. Thirty years later the North West of Africa was rounded. Cape Verde was reached seven years later. By 1448 ships were calling at the Azores. After Henry's death in 1488 the Cape of Good Hope was doubled by Diaz. In 1489 Columbus discovered the West Indian Islands and the New World across the Atlantic and in 1498 Vasco da Gama sailed from Lisbon and crossed the Indian Ocean. In 1493 Pope Alexander VI divided the world by his famous Bull which assigned to Portugal all newly discovered lands to the east of a line running north and south one hundred miles west of the Azores, and to Spain all those lying westward. In 1488, the year of Henry the Navigator's death, Christopher Columbus sent his brother Bartholomew to intreat with the King of England (Henry VII) for the discovery of the Indies. Henry VII accepted the offer but Bartholomew Columbus unluckily fell into the hands of pirates on his way back from England. When he finally returned to his brother it was too late. Christopher had secured the support of Isabella of Spain and set out in 1492 on his eventful voyage. But Henry VII in place of Columbus found Cabot, citizen of Venice, established in Bristol, with the reputation of a skilful mariner and experienced trader. With Cabot's discovery of Newfoundland in 1497 the era of long voyages by English seamen began and the English Merchant Navy came into being. Before Tudor times English sailors had only been coasters save for the crusade of Richard I which took them into the Mediterranean. But this Mediterranean traffic brought English shipping into contact with the mariners of Italy, Spain and Portugal. Chaucer's shipman knew all the harbours from Gothland to Cape Finisterre and every creek in Bretagne and in Spain.

But before the discovery of the New World diseases at sea were scarcely different from those on land. The problems of "Health and Sickness at Sea" came with long voyages of discovery. The need for ship surgeons was quickly realized.

PILGRIM TRAFFIC

The captains undertook to carry a barber-surgeon and a physician and to avoid unhealthy parts. Fynes Moryson advised passengers to take rose leaves, lemons or oranges, or the roots or the leaves of angelica, cloves or rosemary to counteract the evil smells of the boat. This recommendation in 1617 coincides with the publication of Woodall's *Surgeon's Mate*. Woodall probably got his information from Sir James Lancaster, who as early as 1601 had learnt from the Dutch how to prevent and cure scurvy. The following piece of sixteenth century advice is of some slight interest: "At sea remove your spurs: sailors make a point of stealing them from those who are seasick. Keep your distance from them (i.e. the sailors) in any case; they are covered with vermin." Yet in Sebastian Cabot's ordinances for the intended voyages to Cathay in 1553 there is no mention of surgeons being carried. That they were carried we know from a note found, written in one of the two ships (the "Speranza") which wintered in Lappia where Sir Hugh Willoughby and all his company were frozen to death on this voyage. Up to the end of the sixteenth century special galleys ran from Venice to Jaffa for pilgrim traffic.

In the instructions given for a voyage to the East Indies and Cathay, April 9, 1582, Edward Fenton was appointed Captain Generall in charge of three ships with a small frigate or pinnesee, and he was directed to furnish 200 able persons including the gentlemen and their men, the Ministers, Chirurgiens, Factors, &c. When Thomas Candish sailed from Plymouth, surgeons accompanied the expedition.

In the account of the last voyage of Sir Francis Drake and Sir John Hawkins, whilst the ships were watering at the Grand Canary, islanders attacked the shore party and

killed some of them, taking prisoner the surgeon of the ship "Solomon". Later in the voyage James Wood, "chiefe chirurgian of the fleete out of the Garland died". This designation of Wood as chief surgeon of the fleet indicates a fairly advanced degree of medical organization on these expeditions.

During the early part of the eighteenth century voyages of exploration and of privateering under letters of Marque went on apace. One of the best known is that of the "Duke and Duchess" from Bristol, commanded by Woodes Rogers and in which Dr. Dover sailed as Chief Medical Officer with three other surgeons. The voyage is celebrated for its freedom from sickness.

During the eighteenth century many books were published describing the commoner diseases at sea, e.g. Lind, Blane, Clark, Johnson and Trotter.

The East India Company discovered how to send their ships to the East with minimum losses from scurvy. By the end of the eighteenth century they were having their surgeons examined by the Surgeons Company of London and recognized the Diploma of the Edinburgh College of Surgeons. The Charter granted to the Barber Surgeons of London by Charles I in 1629 instructed them to examine the "Sea Surgeons" and compelled any ship sailing from the Port of London to carry a surgeon. Arctic whalers were compelled to carry a surgeon under an Act of Parliament (26 George III c. 41) regulating the Greenland Fisheries.

A few years later (1789) it was enacted (29 George III c. 66) that no Slave Ship should sail unless there was at least one surgeon on board who must produce a certificate of having passed his examination at Surgeons' Hall or at some Publick or County Hospital, or at the Royal College of Physicians or Royal College of Surgeons in Edinburgh.

The first separate Act for regulating passenger ships was 43 George III c. 56. By this Act every vessel carrying fifty persons was required to carry a surgeon possessing a certificate of having passed his examination at Surgeons' Hall, London, or at the Royal College of Surgeons of Edinburgh or Dublin.

The History of the Netherlands East Indies bears witness that the Dutch East India Company tried to maintain an efficient medical service in their Eastern possessions and in their ships sailing to the East. On each ship there sailed two surgeons or even more. These surgeons kept Journals of which some are still preserved.

GENERAL SANITARY MEASURES

General sanitary measures included the problems of fumigation and ventilation, the preservation of drinking water, laundry arrangements and in the Navy and East Indiamen, the provision of a sick berth.

POLAR SEAS

The log books of the two Scoresbys give a record of the Arctic voyages. Those of the elder show that his ship was little troubled with sickness. William Scoresby, Junior, published in 1820 an account of the Arctic Regions, with a history and description of the Northern Whale Fishery. He speaks of the disease prevalent on these voyages, scurvy, frost-bite, intermittents, asthmas and catarrh. Catarrhs, he says, are rarely followed by any dangerous consequences. Fanning, an American skipper, describes the seal fur trade from the South Polar Seas to China and a voyage in the "Aspasia" corvette. They carried an excellent surgeon (Dr. G. Smith of New York City) and Fanning had no sickness in all his voyages except the death of a midshipman from yellow fever. Krusenstern, a Russian Admiral who sailed round the world (1803-1806) gives a poor account of the ships belonging to the American Fur Company that he encountered in the neighbourhood of Kamtchatka. Scurvy was very common on board them and there was great neglect of cleanliness and sanitation among their crews. His own ship, "The Neva", made a voyage lasting over three years, during which time he had amazing good health throughout. Lisiansky, who continued the account of Krusenstern's voyage, speaks of the provisioning of this ship and mentions the various antiscorbutics that were carried. Captain Fanning's voyage is interesting because he mentions that he learnt from the Malays to "sprout" his peas and thereby keep off scurvy.

AFRICAN SLAVE TRADE

The Report of the Lords of the Committee of Council, &c., contains most important evidence of the health of the crews as well as of the slaves. Surgeons were carried to

attend to the health of the slaves and so long as provisions and water did not run short great care was taken of the slaves, and the Surgeon received a capitation payment of one shilling for every slave landed in good health, but he had no responsibility for the officers and crew. Many of the witnesses for the Committee complained of the way the crews were treated. One seaman gave evidence that he was cruelly beaten both by the captain and the surgeon, that he was half starved and that the surgeon neglected the sick seamen, alleging that he was only paid for attending the slaves.

AUSTRALIA

Collins and Browning both bear witness to the careful provision by the Government for the convicts on the ships that sailed to Australia and Van Diemens Land. Sanitation was well looked after and exercise, education, religious instruction, clothing and diet all come under the survey.

WEST INDIES

Although the West Indies had a terrible reputation for sickness the actual voyage to and fro was not exceptionally unhealthy. It was on land and in port that yellow fever made its ravages and gave the "Station" its bad name; but Trotter mentions that communication with the shore produced yellow fever. "The disease," he observed, "uniformly disappeared from ships as they increased their distance from the West Indies. At 32° North no fresh attacks were known." Bancroft, writing in 1811 on yellow fever and other contagious fevers, lays stress on the short distance some contagious fevers could pass over the sea. He gives many quotations showing how short was the distance from shore that the malarial infection could travel and observes that Blane put it at two cables length in Jamaica.

MISSIONARY VOYAGES AND TOURIST TRAVEL

Missionary voyages and tourist travel complete the sum of the voyages belonging to the last part of this account. Wilson's voyage in "The Duff" (1796-98) is one of the best records. He says: "We had run from the time of leaving England upwards of 34,000 miles and had been out fourteen months, eleven of them at sea; yet in all this time we had scarcely experienced any sickness and were at present to a man in good health." It is difficult to obtain a clear impression of ordinary passenger or tourist travel. Such information as we possess comes mainly from private diaries and the sanitary conditions are rarely dwelt upon. Fielding's voyage to Lisbon in 1754 gives a vivid picture of the difficulties of obtaining medical relief, in the first instance for himself when his dropsy required tapping, and in the second place for his wife who tried to get a tooth extracted. Sir Francis Darwin visited Spain and Portugal when the Peninsular War was at its height. He describes some of the perils of the voyage as being intermittent fever at Cadiz, plague at Smyrna, shock from a torpedo-fish whilst bathing and typhus from which his friend Galton died at Malta. His diary also deals with quarantine.

A SCHOOLGIRL'S NOTE

One of the most intimate sketches of sickness on board ship is given in "Letters to Jane from Jamaica". One of Jane's school friends who wrote on March 9, 1792, says: "While the blowing weather lasted we were sadly frightened. Could you have seen us you would have laughed, such a group of figures drawn up in different parts of the cabin, eating off the ground, fed by my brother and the mate, as for the mean sneaking doctor he was such a coward that he kept in bed."

Records in the Older Literature of Tissue Changes in Scurvy

By G. H. BOURNE

(Mackenzie MacKinnon Research Fellow of the Royal College of Physicians of London and the Royal College of Surgeons of England)

"NATURE", said Goethe, "reveals herself best in her abnormalities." In studying the role of vitamin C in the regeneration of bone, or in any of its functions in the body, attention must therefore be paid to that abnormal state which results from the complete deprivation of vitamin C—scurvy. Scurvy is a rare disease to-day, so that to obtain full information of its effects we must turn to the writings of earlier workers who were able to study many cases of the disease.

There is little doubt that scurvy has been known for many centuries. Ebbell (1938) in an analysis of various ancient Egyptian papyri, states that the following hieroglyphs represent scurvy. He provides quite good evidence that the hieroglyphs iv, v, vi, vii and viii indicate a disease characterized by petechial hæmorrhages in the skin. Also, it has been pointed out to the present author that the determinative hieroglyph iii which indicates a little man pointing to his mouth, and the hieroglyph vii which represents blood oozing from a lesion, may indicate that the disease represented by these hieroglyphs is also characterized by bleeding gums. Since bleeding gums and petechial hæmorrhages are characteristic of scurvy, it seems likely that scurvy was known over three thousand years ago in Egypt (the estimated age of the Ebers papyrus from which Ebbell obtained the major portion of his material).

Egyptian hieroglyphs believed to indicate scurvy (*see text*).

Hirsch (1885) has made a critical analysis of the writings of the ancient authors which are presumed to have described scurvy, Hippocrates, Celsus, Aretæus, Caelius, Aurelianus, Paulus, Aegineta and Avicenna. These physicians described a disease called "lines magni" which has been interpreted by various authors (e.g. Guyon, 1846) as scurvy. Hirsch points out that one of the characteristics of this disease is an enlarged spleen which is not a common feature of scurvy, and he believes that the disease described by these ancient authors was, in fact, malaria. Another ancient disease, Pliny's "stomakake", which affected the Roman armies under Germanicus in the Low Countries, is regarded by Hirsch simply as an ulcerative stomatitis, and not as scurvy at all. Another ancient disease, said to be scurvy, was "skeletyrbe", but Hirsch states that Galen's description of the peculiar gait in people suffering from it reminds him of tabetic patients. After a close scrutiny of the literature, Hirsch comes to the conclusion that only in the writings of Hippocrates is there a description of a disease which can unequivocally be regarded as scurvy.

From the cacodoxical attempts of various writers to refer the occurrence of scurvy as far back into antiquity as possible, we come to the far more reliable records of Jacques de Vitry (1873) and de Joinville (1250) of the disease which beset the crusading armies of Louis IX before Cairo. De Joinville mentions blackening of the limbs and fungating gums. The following is his description (taken from Menard's 1617 edition of his writings: the Mediæval French spelling is not altered):

"Et de ce . . . nous vint une grant persecution et maladie en l'ost; qui estoit telle, que la chairdes jambes nous desscheoit jusques à l'os et le cuir devenoit tanne de noir et de terre, à resemblance d'une vieille houze, qui a esté long temps mucée derriere les coffres.

"Et outtre, à nous autres, qui avions cette maladie, nous venoit une autre persecution de maladie en la bouche, de ce que avions mengee de ces poissons, et nous pourissoit la chair d'entre les gencines dont chacun estoit orriblement puant de la bouche."

The outbreak of this disease was thought to be due to the fact that the crusaders ate fish which had fed on the bodies of men killed in battle, floating in a nearby river.

Lind (1753) says that de Joinville's records constitute the first record of true scurvy which he has met with in the ancient literature. The first accounts of scurvy as such were given, according to Lind, by Ronfleus, Echthius and Wierus. Presumably these writers first used the term "scorbutus" or scurvy, but it is not clear either from Lind or from Hirsch who first provided a name for the collection of symptoms which eventually became known as scurvy. Hirsch identifies a disease called by Cordus (who apparently wrote between 1500 and 1600: Hirsch does not quote him in his bibliography) "Scharboch" with scurvy. An epidemic occurring in 1486 was described by Fabricius by this name, according to Hirsch.

Echthius and Wierus gave the most complete descriptions of the disease, which were quoted in detail by subsequent authors, notably Solomon Albertus and Eugalenus. Echthius, according to Lind, described the disease as being characterized by a "spongy swelling of the gums, which are apt to bleed, with a loosening of the teeth: an eruption of leaden-coloured, purple or livid spots on the legs: or of somewhat broader speckled or dark-coloured maculæ, sometimes on the face, at other times on the legs. As the disease advances, the patients lose the use of their legs, and are subject to a difficulty of breathing".

To this description Wierus added that the weakness of the legs "is attended with a stiffness there. The flesh of the gums is often destroyed to the roots of the teeth. Smaller spots, resembling blood sprinkled upon the part (or flea-bites, but larger) appear on the legs, thighs, and on the whole body: . . . in the progress of the disease the tendons of the legs become stiff and contracted. . . . The urine is reddish, turbid, thick and fæculent, like new-red wine. . . . if ulcers break out on the tibia, they are with great difficulty healed up, being extremely fœtid, of a gangrenous disposition. . . ."

Eugalenus (1604) also mentioned, I. Putrid gums; II. Blackish, purple and livid spots; III. Malignant ulcers; as characteristic of scurvy. Many other early authors (see Lind, 1753, for details) have described similar conditions.

Kramer (1720), an Austrian army surgeon, described the disease in the Imperial troops in Hungary and made the interesting observation that the officers did not get it (presumably because of better diet). It is of interest that this has been the case in most armies and often at sea. It was particularly noticeable during the American Civil War. Kramer also mentioned the bleeding, swollen gums and stated that often the teeth fell out. In the second stage of the malady he said that there was apparently a contraction of the joint of the knee because the patient was unable to straighten his leg. The joints became very swollen and painful. Even the eyes were covered with blood spots in some of Kramer's cases. Caries of the jaw was another symptom and so were hæmorrhages from the lungs, stomach and intestines.

In Walter's (1748) account of Lord Anson's voyage round the world it is stated that the constantly occurring symptoms of the disease were "large discoloured spots dispersed over the whole surface of the body: swelled legs: putrid gums: and above all an extraordinary lassitude of the body".

Scurvy decimated both sides in the American Civil War (see Major Charles Smart's *Medical and Surgical History of the War of the Rebellion*, 1888). The army of the Potomac had 30,000 cases of scurvy in five years. Scurvy was more prevalent among the Confederates because their food was worse than that of the U.S. army. The army surgeons in the American Civil War claimed that the characteristic pre-symptom of scurvy in the man was rheumatism. The various conditions found in cases of scurvy during that war were œdematous limbs, stiff and painful joints, petechiæ on the lower extremities, peritoneal, pleural and pericardial hæmorrhages, gums almost totally destroyed, roots of teeth carious, hæmaturia, bloody diarrhœa, large purplish spots (ecchymoses).

In the Crimean war (see *Medical and Surgical History of the British Army in the Crimea*, 1858) Dr. Linton describes "spongy bleeding gums" in the 1st Division before embarkation from Bulgaria for the Crimea. Other surgeons described aching pains in the ankles and feet, purpuric spots on the lower limbs, bleeding from the nose, hæmorrhage from the bowels and hæmatemesis.

According to Sir W. H. Willcox (*Official History of the War*, 1922) cases of scurvy in the last war showed petechial spots, gum changes, hæmorrhages into palate, skin, muscles, joints, periosteum. Pyorrhœa was often present and was said to be a secondary condition of the scorbutic changes.

The first post-mortem examination of persons who had died of scurvy was made during Jacques Cartier's voyage up the Gulf of the St. Lawrence (1535). Post-mortem examinations were also made by Lind (1753) and by Barlow (1894), who identified infantile and adult scurvy. Greater details were given by Aschoff and Koch in 1919, but there are 31 other references to the results of post-mortem examinations of scurvy between Lind's account in 1753 and that of Aschoff and Koch in 1919.

BONE CHANGES IN SCURVY

Lind found that the blood of persons who had died of scurvy did not clot, whether it was left in the body or whether it was withdrawn into a vessel. The lungs were

"blackish and putrid" and the muscles "stuffed with a black corrupted blood". Some bodies when moved could be heard grating and when they were opened the epiphyses of the long bones were found to be entirely separated away. Some persons when alive had been heard to make a "small low noise when they breathed". In these, the cartilages of the sternum were found to be separated from the bony parts of the ribs. In some, the ribs were carious and in nearly all the ligaments of the joints were corroded and loose. Abnormalities in the bones appeared to be a constant feature of scurvy and there are ten publications on post-mortem changes in scurvy between 1883 and 1918 in which only the changes in the bones are described. Lind noted also the presence of what Hess (1920) has subsequently described as "peculiar boggy tumour-like masses of localized œdema", and regarded them as typical of scurvy. He also found that the "breast, belly and several other parts of the body were filled with water or serum". Barlow (1894) wrote also "the muscular walls of the thorax were pale yellow and watery, as though they had been bathed in serum".

Aschoff and Koch and Hess stressed the fact that the characteristic lesions of scurvy are those of the bones. The epiphyses in all young persons have been separated from the bones and in young children there has been found a bending of the ribs, wrongly ascribed (according to Hess) to the effects of vitamin-D deficiency, i.e. rickets, actually the two diseases give different types of beading. Scorbutic monkeys have also been shown to develop beading of the ribs (Hart and Lessing, 1913).

EFFECT OF SCURVY ON THE REPAIR OF TISSUES

Since the earlier evidence suggests that in scurvy there is an upsetting of the normal functioning of both soft and hard tissues, one would expect that repair of injury to any tissue would be delayed in scurvy. That this is a fact can be confirmed further by reference to the older literature.

The earliest known record of the effects of scurvy on wounds is given by Richard Walter (1748), chaplain to Lord Anson's expedition round the world (1740-1744). He made the following comments on this subject.

"At other times the whole body, but more especially the legs, were subject to ulcers of the worst kind, attended with rotten bones, and such a luxuriancy of fungous flesh, as yielded to no remedy. But a most extraordinary circumstance, and what would be scarcely credible upon any single evidence, is, that the scars of wounds which had for many years healed, were forced open again by this violent distemper: of this, there was a remarkable instance in one of the invalids upon the 'Centurion', who had been wounded above fifty years before at the battle of the Boyne: for though he was cured soon after, and had continued well for a great number of years past, yet on his being attacked by the scurvy, his wounds, in the progress of his disease, broke out afresh, and appeared as if they had never been healed: Nay what is still more astonishing, the callus of a broken bone, which had been completely formed for a long time, was found to be hereby dissolved, and the fracture seemed as if it had never been consolidated."

Lind (1753) made the following observation (p. 151): "When one had been confined from exercise by having a fractured bone, or from a bruise or hurt, these weak and debilitated parts become always the first scorbutic." Mr. Ives, writing to James Lind (Lind, 1753, p. 151) of the breaking open of wounds in scurvy, refers to the case of a seaman on H.M.S. "Dragon" who had a shattering of the humerus from a Spanish musket ball. Union of the bone and healing of the skin wounds had been brought about by November, and when in December scurvy broke out on the ship, he fell a victim to the disease, the first symptom being the breaking open of the wounds in his arm. Lind also records that the "slightest bruises and wounds of scorbutic persons degenerate in such ulcers . . . distinguished from all others by being so remarkably putrid, bloody and fungous".

Mead (1762) quoted the case of a sailor who had suffered from a fractured clavicle which had apparently healed normally and which broke again four months later when the sailor was suffering from scurvy. Six months after this, after the sailor had been on a diet of green vegetables for some time, the fracture re-united.

Marrigues (1783), Bell (1788), Callisen (1798) all found softening of the callus of old fractures of bones in scurvy, sometimes with a separation of the ends of the bones. Hammick (1830) reported a number of cases of spontaneous refracture of bones and pointed out that it was impossible to secure the uniting of a fracture so long as the

patient had scurvy. A further example of refracture of a healed broken bone is given by Budd (1840).

Dr. Linton (quoted in the *Medical and Surgical History of the British Army which Served in Turkey and the Crimea,* 1858) described the case of a grenadier aged 23 with a broken humerus. This man broke his arm while carrying a log of wood across some frozen snow. After he had been put in hospital, old ulcers on his leg opened up and his gums became spongy. The callus which formed at the site of the fracture in the humerus was unusually small (suggesting a reduced inflammatory reaction to injury). Only when this man was put on a "good" diet did his fracture unite and his ulcers heal.

Moore (1859) has recorded two cases of fracture of the forearm in which healing was prevented because the patients also had scurvy. Moore stated that this disease has a "powerful effect in retarding the consolidation of fractures".

Major Charles Smart (in the *Medical and Surgical History of the War of the Rebellion*) pointed out that as a result of the scurvy which broke out among the combatant armies of the American Civil War the wounds failed to heal and slight abrasions, such as the rubbing of a shoe, a bruise, the scratch of a mosquito bite, the prick of a splinter, or vaccination scars, tended not only not to heal, but to turn into scorbutic ulcers.

Dr. Eve (1866) stated that in the Confederate Armies during the Civil War the occurrence of scurvy "complicated wounds and seriously interfered with surgical operations". Surgical hæmorrhage was much more frequent as the war progressed.

Even during the last war, Lobmayer (1918) claimed that the Turkish soldiers suffered severely from scurvy and that in those who developed the disease both skin and flesh wounds and fractures healed poorly. In many cases the fractures showed not the slightest sign of the formation of a callus, even after several months. In confirmation of the fact that it was lack of the antiscorbutic substance which was directly responsible for this failure of fractures to unite, he quoted two cases who suffered from pseudo-arthrosis of the humerus and who recovered rapidly and completely as soon as they were put on a diet which was rich in antiscorbutic material.

The study of the older literature of scurvy has thus shown us that the disease is not only characterised by hæmorrhagic symptoms but that there are tissue changes as well, particularly in the bones. There is confirmation too, that scurvy delays the healing of wounds of both skin and bone.

REFERENCES

ANSON, GEORGE, Lord. Voyage Round the World in the Years 1740-4, compiled from his Papers, by Richard Walter, fourth edition. London, 1748.
ASCHOFF, L., and KOCH, W. (1919) Skorbut: eine pathologische-anatomische Studie. Jena.
BARLOW, T. (1894) *Lancet* (ii), 1075.
BELL, B. (1788) A System of Surgery. London, 6.
BIER, A. (1923) *Arch. klin. Chir.,* 127, 1.
—— (1925) *Arch. klin. Chir.,* 138, 107.
BUDD (1840) Quoted by Hertz (1936).
CALLISEN, H. (1798) Quoted by Hertz (1936).
CARTIER, J. (1535) Quoted by Lind (1753).
CELSUS. Quoted by Hirsch (1885).
CORDUS. Quoted by Hirsch (1885).
de JOINVILLE, J. (1250) Writings. New edition by Claud'Menard. Sebastian Cramoisy, Paris, 1617.
de VITRY, J. (1873) Étude histor. et nosol. sur quelques épidémies du Moyen Âge. Paris.
EBBELL, B. (1938) Alt. Ägyptische Bezeichnungen für Krankheiten und Symptomes. Oslo.
ECHTHIUS, J. (1541) Quoted by Lind (1753).
EUGALENUS, S. (1604) Quoted by Lind (1753).
EVE, A. (1866) *see* Medical and Surgical History of the War of the Rebellion, 1888. Washington.
GALEN (*See* Hirsch, 1885).
GUYON, G. (1846) *Gaz. méd. Paris,* 648.
HAMMICK, G. L. (1830) Practical Remarks on Amputations, Fractures and Strictures of the Urethra. London.
HART, C., and LESSING, O. (1913) Der Skorbut der kleinen Kinder. Stuttgart.
HERTZ, J. (1936) Studies on the Healing of Fractures. Oxford.
HESS, A. F. (1920) Scurvy, Past and Present. London.
HIPPOCRATES (*See* Hirsch, 1885).
HIRSCH, A. (1885) Handbook of Geographical and Historical Pathology. Vol. II. The New Sydenham Society. London.
KAPPIS, H. (1927) *Dtsch. med. Wschr.,* 53, 1734.
KRAMER, J. G. (1720) Quoted by Lind (1753).
LIND, J. (1753) Treatise on Scurvy. London.
LOBMAYER, G. (1918) *Dtsch. Z. Chir.,* 18, 203.
MARRIGUES, A. (1783) (*See* Hertz, 1936).
MEAD, R. (1762) Medical Works. London.
Medical and Surgical History of the War of the Rebellion (1888) Vol. I, Part 3, Govt. Printing Office, Washington.
Medical and Surgical History of the British Army which Served in the Crimea. Official account presented to Parliament Session, December 3, 1857; August 2, 1858. Accounts and Papers, Vol. 38, Part II.
MOORE, W. G. (1859) *Brit. med. J.* (i), 447.
Official History of the War (1922) Medical Services, Vol. I. Article on Scurvy by Sir W. H. Willcox.
PLINY (*See* Hirsch, 1885).
WALTER, R. (1748) *see* ANSON, A Voyage round the World, Knapton.
WIERUS, J. Quoted by Lind (1753).

Some Early British Phthisiologists

By Professor S. Lyle Cummins, C.B., C.M.G.

In my opinion the best manner of presenting my subject is to concentrate on a few of those who, taking an untrammelled and original view of tuberculosis, have made definite contributions to it. Doubtless there were many such, but I have decided to deal with only five of them at the present time.

RICHARD MORTON (1637-1698)

Richard Morton was, as far as I can discover, one of the first British physicians to appreciate consumption of the lungs or phthisis pulmonalis as a disease to be closely studied with a view to its cure or amelioration in the living and to be investigated by post-mortem examination in the dead. It is true that, in his work, *Phthisiologia*, he speaks of three kinds of consumption: (1) Original from the whole habit of the body; (2) original consumption of the lungs, and (3) Symptomatical consumption or "such as are the effects of some other Distempers"; in other words, consumptions in all the wasting diseases which human flesh is heir to; but he concentrates upon pulmonary phthisis, "an original consumption of the lungs", as a disease capable of being cured if discovered early and of being ameliorated in most cases, if only for a time, and, therefore, as demanding the closest study.

Richard Morton was the son of the Rev. Robert Morton, Minister of Bewdley Chapel, Worcestershire, from 1635 to 1646. Richard was born in July 1637, two years after his father had taken up the living at Bewdley Chapel. He matriculated at Magdalen Hall, Oxford, on March 17, 1653; passed thence to New College where he obtained his B.A. degree, on January 30, 1656, and became Chaplain to the College. In July 1659 he became an M.A., proceeded as Chaplain of the family of William Foley, Brentwood, Staffs, and was appointed Vicar of Kinver in Staffordshire. He was ejected from his living in 1662 and then took to the study of medicine. He was created M.D. on December 20, 1670, on the nomination of the Prince of Orange. He was admitted as a candidate. for the Royal College of Physicians on January 20, 1679, and he became a Physician-in-Ordinary to the King. He resided at Grey Friars Court, Newgate Street, London, and died on August 30, 1698 (*Dictionary of National Biography*).

Dr. Dawkes (1944) has said that the best way to appreciate the medical history of a disease is to take into account the circumstances of the man who was studying it at the time of observation and to imagine one's self without any of the aids since made available. To do this with reference to Morton and in the case of phthisis, one must assume that the stethoscope does not yet exist, that the microscope is hardly more than the magnifying glass of the child, that radiology is unheard of, that Auenbrugger has not yet introduced percussion and that the knowledge now based on exact information, gathered little by little by all of these means, has not yet been accumulated. Only then shall we be able to appreciate all the difficulties that Morton had to contend with in the study of consumption. Nor was this all. He had also to accept or reject all the theoretical errors as well as the practical successes from the time of Hippocrates onwards. In his favour is the fact that he was not content to accept anything that he could not see or at least that he could not explain in terms of what he had been taught. He did not confine himself to the study of the living; *he also followed up fatal cases by autopsy.*

"The degrees of this Distemper", he says, "are those which follow: to wit, a stuffing of the lungs from the serum or water of the Blood that is plentifully separated in them. Secondly, a hard swelling but more especially in the Glandulous parts of the Lungs arising from the same serum distending those parts too much and not having a free passage out of them; which tumour I take to be the crude Tubercle of Galen; which Tubercles or crude and glandulous swellings I have found on the dead Bodies of Consumptive Persons when other parts of the lungs have been full of Apostemes and Ulcers." What had he been observing? William Bulloch states that in this passage he was following Sylvius and that both proved to be wrong later—*but was he wrong?* He would appear to have based this observation on things that he saw for himself. He was probably speaking of cases which he had observed in young adults dying of semi-primary disease

of the lung; primary disease going on to secondary changes; "glandulous swellings" and "the other parts of the lung . . . full of apostemes and ulcers". Such cases were probably much commoner then than now, when previously uninfected persons from the country districts poured into the great cities and especially London in search of work or pleasure. Though it must be very rarely nowadays that an adult arrives at manifest tuberculosis without having inhaled a certain amount of infection during his childhood this was probably not the case in 1688. I am reminded, in reading his notes, of many post-mortems on Sudanese, on South African natives, on Chinese and others that showed bronchopulmonary and tracheobronchial "glandular swellings" and, in many cases, "apostemes and ulcers" of the lungs as well. They are not often met in Londoners to-day.

But to return to his personal and clinical notes on patients: "The first signs", he says, "which respect a consumption of the Lungs are:

"1. Being born of consumptive parents; for this Distemper (so far as I have been able to observe) is more Hereditary and *oftener propagated from the parents than any other.*"

It was natural for him to call the disease "hereditary" and we may well pardon him that error but we must all agree as to the propagation from father and from mother.

"6 and 7. Long Hypocondriachal Oppressions about the region of the Breast that feel like some troublesome weights . . . thoughtfulness, anxiety, sadness and an unusual proneness to anger, especially if it be without a cause."

These latter points may have a bearing upon the psychology of tuberculosis so often described nowadays.

"9. Spitting of blood *though it be accidental;*
"10. The hawking of black and tough phlegm constantly in a morning for a long time for that it proceeds from these glands being filled with a black Humour which are placed in the lungs near the Windpipe."

Was he talking of coal miners who have black tracheobronchial glands and who spit up a black sputum? Or was he merely noting the darkened spit of those with hæmoptysis? The former is the more likely explanation but the latter may perhaps be the true one.

"13 and 14. A want of Appetite that continues long and grows worse without any other Distemper accompanying it, . . . a troublesome heat, at least in the soles of the Feet and the Palmes of the Hands, together with a pulse somewhat quicker than it ought to be; . . . a disposition to Catarrhs, that is when a sick person is subject to a cough upon very little exertion, yea, and sometimes without evident cause."

What could be better than this description of a tuberculous case? If we put on one side the X-ray film, the physical examination and the pathological investigation, which were then impossible, we find that Morton has mentioned most of the essentials. He goes on: "Therefore in preventing a consumption (which is much easier than the cure of it) the great business, while patients remain in this sickly condition, is to take all possible care that no error be committed in those things which we call natural."

Morton, in the treatment of this stage of consumption, makes free use of opiates at night. "So that it is plainly convenient every night or every other night to give a grain and a half of London Laudenum in a little conserve of Red Roses or an ounce of the Syrup of Meconium with three ounces of Milk-Water . . . or twenty drops of Helmont's Liquid Laudenum in a spoonful of Balsamic Syrup. . . ." He was later followed in this —perhaps quite independently—by Bodington in 1840. He stresses the advice he has just given as to how to retain health. "The great business", he says, "while patients remain in a shaky state is to take all possible care. . . . For in this so slippery a state of Health they are wont upon every occasion of this nature to fall headlong into a Fatal Consumption." . . . "But, alas," he adds, "Physicians have very seldom an occasion to give their advice about preventing this Distemper (when at the beginning it may be cured as well as other diseases although, by neglect, it proves fatal) the sick person seldom imploring Aesculapius' help before the Distemper has run so far as to be a fatal case and then they expect miracles from the Art of Physic when it is more convenient for them to have a good council of a Minister about the future Salvation of their Souls and the advice of a Lawyer about making their last Will."

BENJAMIN MARTEN

A new Theory of Consumptions; more especially of a Phthisis of the Lungs.
London: Printed for R. Knaplock at the Bishop's Head in St. Paul's Church
Yard, etc.—MDCCXXII.

Marten, after a very good opening on the causation, symptoms and signs of a consumption of the lungs, an opening full of his own experiences and with a great many quotations, especially from the work of Morton, proceeds to enunciate a theory of phthisis, a theory which evidently filled his imagination, a theory so thoroughly explanatory of the phenomena of the disease as to appear to us, nowadays, as almost inspired, though passed unnoticed by the Profession at the time; a theory which goes so far to anticipate the subsequent discoveries of Villemin and Robert Koch that it should excite our interest and kindle our imagination. It is true that Reid treated it with amused and indulgent criticism sixty or seventy years after its enunciation but it was so far forgotten that it failed to be mentioned in W. Bulloch's Horace Dobell Lecture of 1910 —though it is mentioned most appreciatively as an extraordinary instance of correct guessing in his *History of Bacteriology* where Bulloch acknowledges his indebtedness for the reference to Charles Singer (1911).

Marten introduces his hypothesis thus: "Concerning the cause of Consumption of the Lungs . . ." others Authors "leave us in the Dark as to the true and original Essence of it; for what the vicious Saltness or Sharpness of the Cattarrhous Humour of the Ancients or the Saltness or some other way viciousness of the Chymist's Tartar or of Helmont's singular and strange Ferment or Sylvious's Salt Acrimony, Willis's Sourness of the Juices, Dolaeus's Sharp Volatile particles, Entmuller's Acrimony and Sharpness of the Blood and Lympha or Morton's Malignant, Ill-natured or Peculiar character of the Humour included in the tubercules or swellings in the Lungs really and essentially are, they have left us at a loss to guess. . . . Some Authors who would account for all Diseases by the doctrine of Acid and Alkali think it sufficient to assert that the Blood, abounding with one or other of these, is the cause of the Consumptions and most other Distempers that affect Mankind; and those who take a peculiar liking to Acids exclaim grievously against what they call a corruptive Alkaline Humour as the patrons of the Alkalis do against a poignant corroding Acid; but this Hypothesis, having lived its time, seems now to be pretty well worn off. But I believe that we must seek some other Primal and Peculiar Cause for this Distemper before we can have a satisfactory idea of it. . . ."

"The original and essential Cause then . . . may possibly be some certain species of Animalcula or wonderfully minute living creature that, by their peculiar shape or disagreeable parts are inimicable to our nature, capable of existing in our Juices and Vessels and which, being drove to the Lungs by the circulation of the Blood, or else generated there from their proper ova or Eggs, with which the Juices may abound or which, possibly being carried about in the Air, may be immediately conveyed to the Lungs by that we draw in and, being there deposited, as in a proper Nidus or Nest, and being produced into Life, coming to Perfection or increasing in bigness may, by their spontaneous Motion and Injurious Parts, stimulating and perhaps gnawing the tender Vessels of the Lungs, cause all the Disorders that have been mentioned." . . . "The Curious, who have not only employed themselves in Philosophical Studies of the vast machinery of the Universe but who also have turned their thoughts upon the admirable Works of Omnipotence in the *Minima Naturæ* and have consequently considered the new World of Wonders that microscopical Observations have opened to our View, will easily conceive the Possibility of very minute organisms being not only the original and Essential Cause of this but of many other Diseases hitherto inexplicable. . . ."

"How Distempers are apparently communicated from one person to another . . . and how they are spread by Degrees and from one County to another may, perhaps, by this Theory, be more easily explained than by any other."

"How the Blood and Juices of some Persons happen to be charged with such Animalcula or their eggs, and the Fluids of other Persons not is next to be enquired into. . . . It seems much more probable that the minute Animals or their Seed which we suppose to be the essential cause of a Phthisis or Consumption of the Lungs are for the most part either conveyed from the Parents to their Offspring or communicated immediately from the distempered Persons to sound ones. . . . The last way, which is properly called infection, we may conceive to be the more reasonable."

of the lung; primary disease going on to secondary changes; "glandulous swellings" and "the other parts of the lung . . . full of apostemes and ulcers". Such cases were probably much commoner then than now, when previously uninfected persons from the country districts poured into the great cities and especially London in search of work or pleasure. Though it must be very rarely nowadays that an adult arrives at manifest tuberculosis without having inhaled a certain amount of infection during his *childhood* this was probably not the case in 1688. I am reminded, in reading his notes, of many post-mortems on Sudanese, on South-African natives, on Chinese and others that showed bronchopulmonary and tracheobronchial "glandular swellings" and, in many cases, "apostemes and ulcers" of the lungs as well. They are not often met in Londoners to-day.

But to return to his personal and clinical notes on patients: "The first signs", he says, "which respect a consumption of the Lungs are:

"1. Being born of consumptive parents; for this Distemper (so far as I have been able to observe) is more Hereditary and *oftener propagated from the parents than any other.*"

It was natural for him to call the disease "hereditary" and we may well pardon him that error but we must all agree as to the propagation from father and from mother.

"6 and 7. Long Hypocondriachal Oppressions about the region of the Breast that feel like some troublesome weights . . . thoughtfulness, anxiety, sadness and an unusual proneness to anger, especially if it be without a cause."

These latter points may have a bearing upon the psychology of tuberculosis so often described nowadays.

"9. Spitting of blood *though it be accidental;*
"10. The hawking of black and tough phlegm constantly in a morning for a long time for that it proceeds from these glands being filled with a black Humour which are placed in the lungs near the Windpipe."

Was he talking of coal miners who have black tracheobronchial glands and who spit up a black sputum? Or was he merely noting the darkened spit of those with hæmoptysis? The former is the more likely explanation but the latter may perhaps be the true one.

"13 and 14. *A* want of Appetite that continues long and grows worse without any other Distemper accompanying it, . . . a troublesome heat, at least in the soles of the Feet and the Palmes of the Hands, together with a pulse somewhat quicker than it ought to be; . . . a disposition to Catarrhs, that is when a sick person is subject to a cough upon very little exertion, yea, and sometimes without evident cause."

What could be better than this description of a tuberculous case? If we put on one side the X-ray film, the physical examination and the pathological investigation, which were then impossible, we find that Morton has mentioned most of the essentials. He goes on: "Therefore in preventing a consumption (which is much easier than the cure of it) the great business, while patients remain in this sickly condition, is to take all possible care that no error be committed in those things which we call natural."

Morton, in the treatment of this stage of consumption, makes free use of opiates at night. "So that it is plainly convenient every night or every other night to give a grain and a half of London Laudenum in a little conserve of Red Roses or an ounce of the Syrup of Meconium with three ounces of Milk-Water . . . or twenty drops of Helmont's Liquid Laudenum in a spoonful of Balsamic Syrup. . . ." He was later followed in this —perhaps quite independently—by Bodington in 1840. He stresses the advice he has just given as to how to retain health. "The great business", he says, "while patients remain in a shaky state is to take all possible care. . . . For in this so slippery a state of Health they are wont upon every occasion of this nature to fall headlong into a Fatal Consumption." . . . "But, alas," he adds, "Physicians have very seldom an occasion to give their advice about preventing this Distemper (when at the beginning it may be cured as well as other diseases although, by neglect, it proves fatal) the sick person seldom imploring Aesculapius' help before the Distemper has run so far as to be a fatal case and then they expect *miracles* from the Art of Physic when it is more convenient for them to have a good council of a Minister about the future Salvation of their Souls and the advice of a Lawyer about making their last Will."

BENJAMIN MARTEN

A new Theory of Consumptions; more especially of a Phthisis of the Lungs.
London: Printed for R. Knaplock at the Bishop's Head in St. Paul's Church
Yard. etc.—MDCCXXII.

Marten, after a very good opening on the causation, symptoms and signs of a consumption of the lungs, an opening full of his own experiences and with a great many quotations, especially from the work of Morton, proceeds to enunciate a theory of phthisis, a theory which evidently filled his imagination, a theory so thoroughly explanatory of the phenomena of the disease as to appear to us, nowadays, as almost inspired, though passed unnoticed by the Profession at the time; a theory which goes so far to anticipate the subsequent discoveries of Villemin and Robert Koch that it should excite our interest and kindle our imagination. It is true that Reid treated it with amused and indulgent criticism sixty or seventy years after its enunciation but it was so far forgotten that it failed to be mentioned in W. Bulloch's Horace Dobell Lecture of 1910 —though it is mentioned most appreciatively as an extraordinary instance of correct guessing in his *History of Bacteriology* where Bulloch acknowledges his indebtedness for the reference to Charles Singer (1911).

Marten introduces his hypothesis thus: "Concerning the cause of Consumption of the Lungs . . ." others Authors "leave us in the Dark as to the true and original Essence of it; for what the vicious Saltness or Sharpness of the Cattarrhous Humour of the Ancients or the Saltness or some other way viciousness of the Chymist's Tartar or of Helmont's singular and strange Ferment or Sylvious's Salt Acrimony, Willis's Sourness of the Juices, Dolaeus's Sharp Volatile particles, Entmuller's Acrimony and Sharpness of the Blood and Lympha or Morton's Malignant, Ill-natured or Peculiar character of the Humour included in the tubercules or swellings in the Lungs really and essentially are, they have left us at a loss to guess. . . . Some Authors who would account for all Diseases by the doctrine of Acid and Alkali think it sufficient to assert that the Blood, abounding with one or other of these, is the cause of the Consumptions and most other Distempers that affect Mankind; and those who take a peculiar liking to Acids exclaim grievously against what they call a corruptive Alkaline Humour as the patrons of the Alkalis do against a poignant corroding Acid; but this Hypothesis, having lived its time, seems now to be pretty well worn off. But I believe that we must seek some other Primal and Peculiar Cause for this Distemper before we can have a satisfactory idea of it. . . ."

"The original and essential Cause then . . . may possibly be some certain species of Animalcula or wonderfully minute living creature that, by their peculiar shape or disagreeable parts are inimicable to our nature, capable of existing in our Juices and Vessels and which, being drove to the Lungs by the circulation of the Blood, or else generated there from their proper ova or Eggs, with which the Juices may abound or which, possibly being carried about in the Air, may be immediatly conveyed to the Lungs by that we draw in and, being there deposited, as in a proper Nidus or Nest, and being produced into Life, coming to Perfection or increasing in bigness may, by their spontaneous Motion and Injurious Parts, stimulating and perhaps gnawing the tender Vessels of the Lungs, cause all the Disorders that have been mentioned." . . . "The Curious, who have not only employed themselves in Philosophical Studies of the vast machinery of the Universe but who also have turned their thoughts upon the admirable Works of Omnipotence in the *Minima Naturæ* and have consequently considered the new World of Wonders that microscopical Observations have opened to our View, will easily conceive the Possibility of very minute organisms being not only the original and Essential Cause of this but of many other Diseases hitherto inexplicable. . . ."

"How Distempers are apparently communicated from one person to another . . . and how they are spread by Degrees and from one County to another may, perhaps, by this Theory, be more easily explained than by any other."

"How the Blood and Juices of some Persons happen to be charged with such Animalcula or their eggs, and the Fluids of other Persons not is next to be enquired into. . . . It seems much more probable that the minute Animals or their Seed which we have supposed to be the essential cause of a Phthisis or Consumption of the Lungs are for the most part either conveyed from the Parents to their Offspring or communicated immediatly from the distempered Persons to sound ones. . . . The last way, which is properly called infection, we may conceive to be the more reasonable."

Marten knew all about the cause of Scabies or Itch[1] and he had come to the conclusion that venereal disease, at any rate, was communicated from person to person by contact. "We find some Diseases are apparently communicated from one person to another by Contact or Touch only, of which the Itch and the Venereal Distemper are eminent instances; that the essential cause of the former disease is a vast number of minute Animals that, by their Spontaneous Motion and injurious parts, make furrows under the Epidermis or Scarf Skin, may be demonstrated by viewing through a good Microscope a small portion of the Humour contained in the little Bladders that arise in this Distemper between the Fingers, etc. . . ."

As to the treatment of tuberculosis, Marten advocates many things but especially speaks as follows: "Where People labouring under this Distemper are continually sitting still, musing on or lamenting their own sikly condition . . . they take a ready way to promote the Distemper instead of their own Health. . . . Whereas those who exert themselves and make use of what remaining strength they have in proper Exercise . . . cannot humanly speaking fail of recovering their pristine Health and Strength. . . . And, of all others, that of riding on Horseback in the manner of Travellers and not too furiously is certainly the most excellent."

WILLIAM STARK (1741-1770)

William Bulloch, in his Horace Dobell Lecture on November 10, 1910, a lecture which dealt with "The Problem of Pulmonary Tuberculosis", referred to the work of "William Stark, a young Physician of St. George's Hospital, whose untimely death at the age of 29, brought about by experiments on his own body, robbed English pathology of one of its earliest and most accurate observers". There is no doubt that Bulloch was right in his assessment of Stark as one of the earliest and most accurate of British pathologists, nor is there any doubt that he was a physician of St. George's Hospital, yet it is a curious fact that St. George's Hospital has now no trace of this brilliant experimentalist in its notes of former distinguished St. George's men. The reason would appear to be that Stark studied first in Glasgow and then in Edinburgh and that he only came to London and to St. George's later on. He was never strictly a student there if we are to accept the rather limited idea of a student as a neophyte in the study of a profession. He had been a neophyte in Glasgow and in Edinburgh but it seems that he was only a very keen and enthusiastic seeker after truth when he came to St. George's in the year 1765 and now "devoted himself to the study of physic" (Dr. Carmichael Smith's Preface to the works of Stark, 1788).

There is no doubt that he was very well known to his colleagues at St. George's at that time and was remembered there for long after his death. Matthew Baillie seems to have completely confirmed his work in 1793 and the name of the latter is coupled with his by Bulloch as one of the founders of the studies underlying "the modern era of tuberculosis".

It is sad to see so much learning and so much endeavour now quite forgotten amongst the very scenes where it was acquired; but it is comforting to remember that the knowledge itself was well used by a number of brilliant St. George's men in after years. No hospital has contributed more generously to our understanding of tuberculosis than St. George's itself.

To Dr. Carmichael Smith, another St. George's man, we owe the publication of Stark's works in 1788. Without his valuable assistance in this matter they might have gone unpublished and we should be so much the poorer in this respect. In his Preface, he gives the following brief biological notes: "Stark's father, as I have been told, was a native of Ireland, his mother of Scotland; he himself was born in Birmingham." . . . "But, wherever his cradle was rocked he was educated at Glasgow and there, under Drs. Adam Smith, Black, Reid, etc., he first learnt the rudiments of philosophy. . . ." "From Glasgow he repaired to Edinburgh where he was soon distinguished and honoured with the friendship of Dr. Cullen" . . . "Having finished his studies at Edinburgh he came to London in the year 1765 and now devoted himself to the study of Physic and, looking upon anatomy as one of the pillars of the Art, he endeavoured to complete, with Dr. John Hunter, what he had begun with Dr. Munro and acquired under this

[1] This had been known in England through the work of Thomas Moffet. Book 1539, now in Brit. Museum. (Charles Singer.)

eminent Professor that perfect anatomical knowledge which appears in all his dissections. He likewise entered himself a pupil at St. George's Hospital and, disgusted as he often told me, with the inaccuracy and want of candour of the generality of practical writers, he determined to obtain an acquaintance with diseases at the latter School and under an abler master; and to have, from his own experience, a standard by which he might judge the experience of others." . . . "In 1767 he graduated at Leyden and published an inaugural Dissertation on Dysentery. On his return to London he recommenced his studies at the Hospital and in June 1769 began his Experiments on Diet, to which undertaking he was greatly encouraged by Sir John Pringle and Dr. Franklin, whose friendship he then enjoyed, and from whom he received many hints, both as to the plan and afterwards in the execution of his design. These experiments, or rather the imprudent zeal with which he prosecuted them, proved in the end fatal to himself; at least such was the general opinion of his friends at the time but, to my mind, and I speak from intimate knowledge of his character, other causes, particularly chagrin and disappointment, had no small share in bringing about the event." . . . "Dr. Stark·was much more conversant with books than with men. . . . He was ill prepared for the cold prudence, the time-serving meanness or the base duplicity which he met with in others . . . nor had he yet made the observation of Figaro, equally applicable to all ages and to all countries:

> 'que le savoir faire vaut mieux que le savoir.' "

     •   •   •   •   •   •

What did Stark do for our knowledge of tuberculosis? To me it seems that he did much. At a time when the great majority of doctors was content to study the gradual march of the disease from its diagnosable first stages to its final break-down into a fatal illness he made the essential first studies which were destined to lead pathologists and, finally, clinicians to perceive that the disease might, in some cases, be amenable to cure. Others had, it is true, seen tubercles in the lungs and had noted the presence of "apostemes" and "ulcers" as part of the disease complex, but Stark was the first to examine minutely·the growth and development of these little tumours and to show how they might gradually lead to advanced disease and death. Let him speak for himself.

"In the cellular substance of the lungs are found roundish firm bodies, of different sizes, from the smallest granule to about half an inch in diameter, the latter often in clusters. The tubercles of a small size are always so; even those of a larger are frequently so; they are of a whitish colour and of a consistence approaching to the hardness of cartilage; when cut through, the surface appears smooth, shining and uniform. No vesicles, cells or vessels are to be seen in them, even when examined with a microscope, after inspecting the pulmonary artery and vein. On the cut surface of some tubercles were observed small holes as if made by the pricking of a pin; in others were found one or more cavities containing a thick white fluid like pus; at the bottom, also, of each of these cavities, when emptied, several small holes were frequently to be seen from which, on pressing the tubercle, matter issued; but neither these holes nor any others above-mentioned (so far at least as could be determined) communicated with any vessels. . . . The cavities, in different tubercles, are of different sizes, from the smallest perceptible to half an inch in diameter and, when cut through and emptied, have the appearance of small white cups, nothing remaining of the substance of the tubercle except a thin covering or capsule." "The cavities of less than half an inch in diameter are always quite shut up; those which are a little larger have, as constantly, a round opening made by a branch of the trachea. At this period, there being a free passage for the matter contained in the tubercle into the trachea and a communication between the cavity of it and the open air, it is proper to change the name of the tubercle to that of vomica."

"The smaller vomicæ are commonly entire, the larger are frequently ruptured; the largest (which, generally speaking, are of an oval shape and about four inches in length), are lined, either partially or entirely, with a smooth, tender slough or membrane: the same as the capsula of the smaller vomicæ. The matter contained in them, when the capsula is entire, is whitish or yellowish; when ruptured reddish, . . . in either case readily diffusible in water. It is proper, however, to remark that, even in the largest vomicæ, when they are not completely ruptured, the matter is seldom red but yellowish, ash-coloured or greenish; often fœtid. . . . Into all the vomicæ, the smallest excepted, there are several openings of the bronchia; also openings forming communications between the different vomicæ. The bronchial openings are commonly round and smooth, the

others generally irregular and ragged. The larger vomicæ, which have numerous bronchial openings, are found to contain scarcely more matter than is sufficient to besmear their surface; and what shows clearly that the matter is discharged by these openings of the aspera arteria is that if a deep incision be made into any diseased part of the lungs, and that part gently compressed, the matter will be seen to issue from the cut extremities of the bronchia; or if any considerable branch of the aspera arteria be laid open and the lungs pressed in the same manner, the matter will be seen coming into it from the smaller ramifications." . . . . "Where ever there is a vomica there is always a broad and firm adhesion of that part of the lungs to the parietes or pleura so as to preclude all communication between the cavity of the vomica and that of the chest; even tubercles are seldom without adhesion "

"The pulmonary artery and veins, as they approach the larger vomicæ, are suddenly contracted; a blood vessel which, at its beginning, measured nearly half an inch in circumference sometimes, though it had seen off no considerable branch, could be cut up no farther than an inch; and when, outwardly, they are of a larger size, yet internally they have a very small canal, being almost filled up by a fibrous substance; and, frequently, as they pass along the sides of the vomicæ, they are found quite detached for about an inch of their course from the neighbouring parts. That the blood vessels thus are obstructed and that they have little or no communication with the vomicæ, is rendered still more evident by blowing into them or injecting them; by blowing into them they are not swiftly distended nor does air pass into the vomicæ except very rarely and then only by some imperceptible holes, and, after injecting the lungs by the pulmonary artery and vein, the parts less affected by disease, which before injection were the softest, become the hardest and *vice versa*, the most diseased parts, before injection, the hardest, are now the softest. . . . The wax was very rarely found to have entered the middling sized vomicæ and never the smaller or larger ones."

"*State of the air vesicles and cellular substances.*—Those parts of the lungs which are contingent to tubercles are red, sometimes soft, but more frequently firm and hard; and, while other parts of the lungs unaffected by disease are readily distended by blowing into the trachea, those parts which are contiguous to tubercles or vomicæ remain depressed and impervious to air, either blown into the lungs in this manner or forced, by a blow pipe, into incisions made on the surface. So that the function of the lungs, so far as respects the admission of air, seems, in those parts, entirely destroyed."

Stark gives an excellent summary of the symptoms of the disease but I think I have quoted him sufficiently to show what a pathologist was able to do towards the unravelling of the tangled skein of tuberculosis in 1769.

GEORGE BODINGTON (1799-1882)

In George Bodington we have the very mirror of an Englishman; a sensible, gallant man prepared to face martyrdom or enthusiastic recognition equally as a matter of little consequence if only he might say openly that what he had *observed* as to tuberculosis was literally *true* because *seen* by him. He got his martyrdom during his life and his enthusiastic recognition after his death; a not uncommon happening to one endowed with the gift of prophecy! He was, as the *Lancet* of March 11, 1882, said of him, "the descendant of one of the old yeoman families of Warwickshire, the Bodingtons of Cubbington, who had tilled their own land in that parish since the time of Henry VIII". He was sent to Magdalen College School, Oxford, and, from there, went as an apprentice to a surgeon at Atherstone, a Mr. Syer. Later, he became a student at St. Bartholomew's Hospital and qualified as a medical practitioner in 1825. He then transferred to Birmingham and, afterwards, to Erdington where he practised until 1843. In that year he proceeded to Driffield House Asylum, Sutton Coldfield, of which he had become the

proprietor in 1836, with the idea of devoting his life to the treatment of the insane. He must have continued to practise general medicine, however, as patients suffering from tuberculosis continued to seek his advice. His pamphlet on *The Treatment and Cure of Pulmonary Consumption* was published in 1840 and is a notable contribution to our knowledge of the disease.

He was the first not merely to advocate but to treat patients suffering from phthisis by giving them plenty of good, fresh air, a sufficiency of wholesome food and a definite quantity of wine, with a sedative, opium, to ensure sleep and calm apprehension as and when necessary. And, above all, he asked that they should be taken into a house specially prepared for them and kept under the eye of a specialist in the management of tuberculosis. The *Lancet* of July 1840, spoke of this rather revolutionary essay as follows:

> "The modest and rational preface with which the author introduces us to his pamphlet on pulmonary consumption has so far influenced us that we shall merely give an outline of his principles without expending any portion of our critical wrath on his very crude and unsupported assertions."

What was it that the *Lancet* found so crude? "So soon as the nervous power is entirely destroyed in those portions of the lungs where the tuberculous deposits exist, then the destruction of the remaining tissues follows immediately;" on the other hand "tuberculous matter is often found deposited upon sound lungs where it has been rendered harmless by a vigorous state of nutrition and the sanguiferous system." In a consumptive patient we shall find "first of all, a rapid and weak pulse ranging from 120 to 140 beats a minute. . . . This condition must be met at once" not by antiphlogistics "but with frequent supplies, in moderate quantities, of nourishing diet and wine; a glass of good sherry or madeira in the forenoon with an egg, another glass of wine after dinner, some nourishing food for supper, etc.". "I have generally succeeded in the course of a few days . . . in reducing the pulse from 130 or 140 down to 90", and, as to sedatives, "the direct or full dose is given at bed time to allay coughing and to produce sleep" . . . "I come now to the most important remedial agent in the cure of consumption, that of the free use of a pure atmosphere." "The air out of doors early in the morning either by riding or walking" . . . "with intervals of walking as much as the strength will allow of, gradually increasing the length of the walk until it can be maintained easily several hours a day." . . . "The abode of the patient should be in an airy house in the country; if on an eminence so much the better; the neighborhood should be dry and high; the soil a light loam, a sandy or gravelly bottom; the atmosphere is, in such situations, comparatively free from fog and dampness." He speaks of the value of open air . . . "Thus the equal temperature so much considered and said to be necessary should be that of the external air instead of that so commonly employed, the warmth of a close room." He tried this treatment by admitting patients under his own roof and there giving them the advantages noted. "In those cases which I have treated upon these principles having had some of the patients under my own roof, by which I secured all the advantages of situation, etc. before spoken of, and some in my immediate neighborhood, so that I could closely watch them, I have met with signal success." He describes six cases which were so very successful that one is tempted to ask one's self whether he was not observing the great improvement which usually comes on after admission to either hospital or sanatorium—but he steadily followed his cases up when possible and one must admit that he had signal success. "The generality of the medical profession," he says, "have not the opportunity of thus treating their consumptive patients; if they are to succeed, they should have country houses in proper situations, well ventilated, and provided with all 'appliances and means to boot' where their patients should be under their own eyes and strictly watched and regulated in all respects as regards exercise, air, diet, medicine, etc., or there should be a certain class of practitioners who should exclusively pursue this practice as a distinct branch to whom those in large towns should confide their consumptive patients instead of sending them, as many do now, to take their chance or probably fall into the hands of mercenaries at some distant sea port where they commonly die, far away from friends and home." He adds that he has, to carry out this treatment, "taken for the purpose a house in every respect adapted and near my own residence, for the reception of patients of this class who may be desirous or who are recommended to remove from their homes for the benefit of the change of air".

In other words, Bodington not only saw a vision but actually put the means thereof into practice. He was howled down by the medical profession of his day but he now stands for the system which at last is bringing the curse of tuberculosis under control.

WILLIAM BUDD, M.D.

Memorandum on the Nature and the Mode of Propagation of Phthisis.
Lancet, p. 452, October 12, 1867

William Budd was a man to whom the appearances, symptoms and characters of pulmonary phthisis were well known for he had been for a long time in practice at Clifton and Bristol to which places many phthisics repaired and to which, in an especial degree, the negroes employed on our ships came for treatment when they found themselves unable to continue work owing to the ravages of pulmonary consumption. He was therefore in a very good position to compare the chronic phthisis of Europeans and the swift and usually fatal form occurring in the blacks. We may imagine that he had meditated often on the differences between these two types and had been greatly puzzled by them yet without a clue until that great day when enlightenment came to him. "The idea that phthisis is a self-propagating zymotic disease and that all the leading phenomena of its distribution may be explained by supposing that it is disseminated through specific germs contained in the tuberculous matter cast off by persons already suffering from the disease *first came into my mind unbidden, so to speak, while I was walking on the Observatory Hill at Clifton in the second week of August* 1856." With this idea came the sequel : "The Geographical distribution of phthisis in past and present times and especially its great fatality in countries which, when first discovered (by Europeans) were absolutely free from it." . . . "When the South Sea Islands were first discovered, phthisis did not exist there," and it was now very prevalent. . . . "Now, everywhere along the African sea-board, where the blacks have come into contact and intimate relations with the whites, phthisis causes a large mortality among them. In the interior, where intercourse with has been limited to casual contact, . . . there is reason to believe that phthisis does not exist." This observation—and how true it was— came into his mind at about the same time that it entered the mind of Villemin, that great Frenchman who was to use it to demonstrate by the experimental method upon the bodies of rabbits and guinea-pigs the literal truth of it. How came it that, in the Englishman, it went no further than an illuminating idea? Budd was a general practitioner with all his notions held in check by the exigencies of his patients. Villemin, on the other hand, was a Professor at the French Army Medical College at the Val de Grâce, with great opportunities for research at his disposal. In both there was the same rich and productive brooding over a common and terrible disease seen with eyes stripped of all convention; in both, there was the same response, an intuitive motion towards the truth. It was as if two duelling pistols had been prepared and only one loaded! When the triggers were pulled, in both there was the flash in the pan. In the unloaded, the matter stopped there. In the loaded the charge was exploded and the bullet sent to fell its victim—the swollen bulk of authoritarian theory which was holding the minds of the profession in thrall! The result, then, was different. In the one case it eventuated in a letter to the *Lancet*—which was soon forgotten! In the other the theory of a microbic origin for phthisis was converted into the established fact that caseous material from the human, or better the bovine, could produce in the rabbit a wasting and often fatal disease which was capable of being transmitted through animal after animal with the regularity of clockwork. It was reserved for Robert Koch to demonstrate the essential cause twenty years later and to focus the activity of all laboratory workers on the acid-fast bacillus which is the cause of tuberculosis.

Section of Anæsthetics

President—R. J. MINNITT, M.D., D.A.

[*May 5, 1944*]

Machines for Regional Analgesia

By NORMAN R. JAMES, L.R.C.P.E., D.A.

EVER since the introduction of practical methods of regional analgesia during the latter part of the last century, numerous machines have been constructed with a view to replacing the syringe with its many disadvantages.

On November 3, 1900, Rudolph Matas described in the *Philadelphia Medical Journal* a simple type of infiltrator used to inject weak solutions of cocaine. Lantern slides showing the subsequent development of infiltrators were then shown, concluding with an infiltrator devised after two years experimenting with the help of the Medical Research Council. We have eliminated the defects in the earlier machines shown and the apparatus is: (1) safe to operate (automatic safety trap); (2) of robust construction, stainless steel being used extensively; (3) portable; (4) easily sterilized and charged. (5) It has a large capacity of 5 litres.
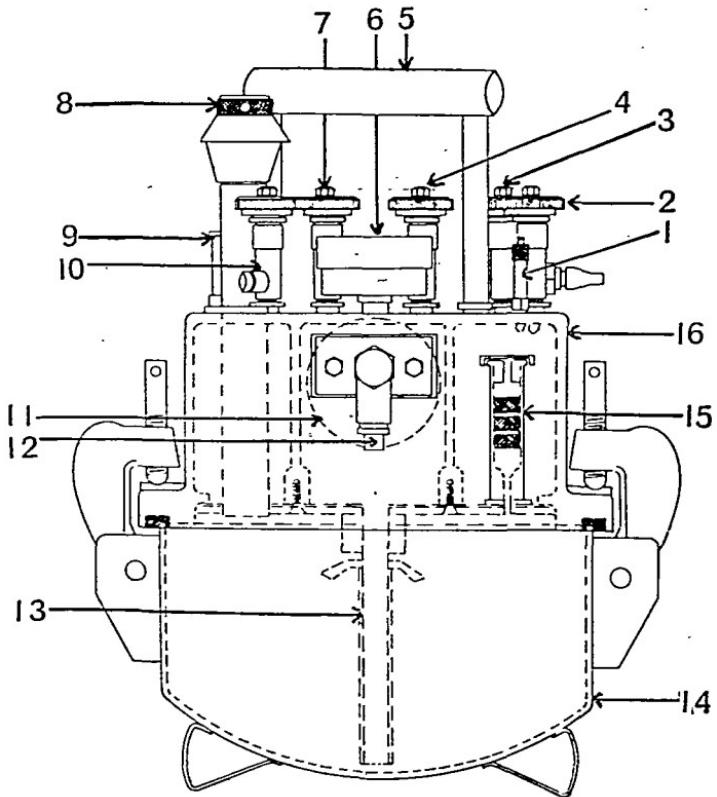
1. Schrader connexion for foot pump for use when compressed gases are not available.   2. Pressure intake control valve when compressed gases are available.   3. Filter sump outlet valve.   4. Supply control valve No. 1 for analgesic solution.   5. Lifting handle.   6. Combined vacuum and pressure gauge.   7. Supply control valve No. 2 for analgesic solution.   8. Swing-over filler cap for recharging machine with analgesic solution. 9. Pressure safety valve.   10. Steam inlet control valve for sterilization.   11. Ball-float for operating automatic safety trap to ensure that the compressed gas cannot be injected when the supply of the solution is exhausted. 12. Automatic valve to maintain vacuum after steam sterilization.   13. Solution uptake pipe from reservoir. 14. Stainless steel reservoir polished to mirror finish.   15. Compressed gas intake filter fitted with ultra-fine replaceable fabric filtration cartridges.   16. High tensile bronze casting.

All components unless of stainless steel are chromium plated.   Dimensions (overall): height, 14 in.   Diameter 10¼ in.

No means of measuring the dosage is provided, as our experience has shown that when weak solutions are used the dosage is of no account. An aspirating device worked by an injector may if wanted be attached to the pistol.

In conclusion we believe that this infiltrator should prove of special service to those who use infiltration analgesia as a routine in thoracic, cranial, and plastic surgery.

Major S. Rowbotham drew attention to three points of great importance:

(1) Dosage: 300 milligrammes was considered the maximum dose of amethocaine and even in great dilution this amount should not be exceeded. In his own experience in thyroid cases he had observed signs of absorption—restlessness and tachycardia—when using a greater dilution than James recommended, i.e. 1:4,000, and a total quantity never in excess of 150 c.c.

(2) It was important to be able to produce suction whenever infiltration was performed below the subcutaneous tissues.

(3) Adrenaline: Even in extreme dilution, in his opinion, quantities over 0·5 c.c. of the 1:1,000 solution might produce dangerous symptoms. In using unlimited quantities of the anæsthetic solution it was most important that the amount of adrenaline which the patient was receiving should always be kept in mind.

Some Toxic Effects following Trilene Decomposition Products
(*Précis*)

By Margaret McClelland, M.B., B.S., D.A.

During four months of last summer thirteen patients developed cranial nerve palsies following a variety of general anæsthetics. The degree of severity varied from subjective trigeminal anæsthesia only to a complete picture of encephalitis in one of the patients who died. The nerves involved were Vth with VIIth in many, and in some IIIrd, VIth, VIIIth, Xth, or XIIth. Herpes of the febrile type developed about the third day in eleven of the patients. The only abnormalities in the cerebrospinal fluid were in two cases a small increase in polymorph cells and in five an increase in protein.

The outstanding post-mortem finding in the patient who developed a picture of encephalitis was œdema of the brain and brain-stem although there were occasional localized perivascular collections of lymphocytes.

The earliest approach to the problem of investigation was an analysis of anæsthetic drugs but as there were no impurities apart from a trace of chlorine in the cyclopropane, and this within the specifications of the U.S.P., the possibility of a virus infection was considered.

Virus theory.—Although the incubation period was short for a virus infection the post-mortem findings were not inconsistent with an encephalitis and were comparable with some of the findings in the encephalitis lethargica epidemic after the last war. Isolation of herpes virus during this epidemic was claimed by Doerr and Berger in 1922 and Flexner and Amoss in 1925.

Andrewes, Carmichael and Brain showed that 75% of hospital patients have antibodies to herpes in the blood, and in the majority overt lesions can be produced by artificial hyperthermia, intravenous T.A.B. vaccine, &c.

Herpes occasionally occurs after an infection of the gasserian ganglion (Harris). All our cases, including those who did not develop herpes, had antibodies in the blood. Keddie *et al.*, treating patients by artificial fever therapy, states that 80% of them develop herpes in one to three days, but temperatures taken in the machine and of the patient before and after anæsthesia, did not substantiate a theory of hyperthermia.

Animal Inoculations.—A large number of animals were inoculated by Dr. Humphrey at the hospital and by Dr. Andrewes of the National Institute for Medical Research. No evidence of transfer of a virus infection was obtained.

There is some experimental evidence of a virus infection being "lit-up" by an anæs-thetic. Fiala, in 1943 observed that subdural or intravenous injection of vaccinia virus is not normally followed by encephalitis, but is so if the animals are under arethane anæs-thesia.

In the absence of any positive findings in the animal inoculations, it is only possible to suggest that herpes virus played a part.

Anæsthetics.—The anæsthetics were extremely varied; trilene was used on only two cases—the remainder receiving combinations with pentothal, nitrous oxide, ether and cyclopropane. It was notable that all the cases occurred in one of the two major opera-

ing theatres and all on the same type of machine, this being one on which either a simple "semi-open" method or else a closed circle carbon-dioxide absorption technique may be used. There is only one bottle on the machine and it contains a gauze wick which retains a little of whatever drug has been in the bottle previously and thereby contaminates the drug next used. In the other theatre a simple Boyle machine is used and on it there were no cases. During the period under review 600 inhalation anæsthetics were administered in the theatre where all the cases occurred and 340 in the other theatre. 15% received trilene.

Reports by Hewer and McAuley (1943) of Vth nerve palsies associated with trichlorethylene anæsthesia, by Stuber (1931) in German industry and the further observations (Morton, Stuber, Browning) that chemical reactions may occur between trichlorethylene and alkalis put this drug under suspicion. It is conceivable that when trilene was used by the "to and fro" technique some might linger in the machine on the gauze wick and be carried over into the absorber when a subsequent anæsthetic was given. The sodalime used was a hygroscopic brand containing 11·2% of sodium hydroxide and temperatures up to 160° F. were recorded during its use. The frequent occurrence of an unusual penetrating odour about the machine led to the suspicion that some toxic agent was being formed.

Chemistry.—Dr. H. E. Cox, D.Sc., F.I.C., to whom the machine and samples of the drugs used were sent, considered there were several conditions suggestive of chemical change: (1) The sour smell noted in our soda-lime; (2) the high temperatures generated in the soda-lime; (3) all the rubber parts are likely to contain fillers and anti-oxidants. Rubber is porous to cyclopropane and is also affected by ether and trilene, so it is apparent there are possibilities for chemical change, particularly when it is remembered that cyclopropane contains a short carbocyclic ring which is easily opened to form an unsaturated hydrocarbon, and trilene has a double bond as well as an active halogen. Another reason for suspecting chemical reactions was the irregular incidence of the toxic symptoms.

His investigations revealed no impurities in the ether, trilene or cyclopropane nor reactions between them. Reactions producing a distinctive smell occurred with trilene and soda-lime, slowly at room temperature and rapidly at blood heat. The temperature is important. Trilene can produce potentially toxic substances in two ways:

A.
$$CHCl \!=\! CCl_2 \text{ (trilene)} + NaOH \longrightarrow CCl \!\equiv\! CCl \text{ (dichloroacetylene)} + NaCl + H_2O$$

B.
$$CHCl \!=\! CCl_2 \text{ (trilene)} + O_2 \longrightarrow \underset{\text{(trichloroethylene-ether)}}{CHCl\!-\!CCl_2 \text{ with } O} \longrightarrow CHCl_2 \quad COCl \text{ (dichloroacetyl-chloride)}$$
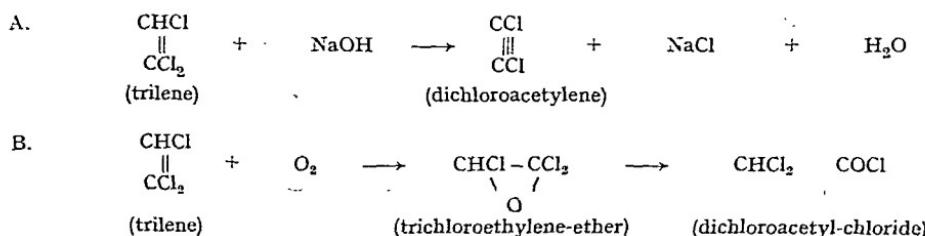
The result of reaction A is dichloroacetylene which is easily oxidized to phosgene, carbon monoxide and carbon dioxide, but this does not take place in the presence of excess trilene. Further confirmation is obtained by the presence of sodium chloride in the soda-lime.

Examination of our soda-lime used revealed 0·05% of NaCl which, on the quantity in the bottle, is equivalent to about 0·6 g. of dichloroacetylene on the 500 g. of soda-lime. Various experiments revealed dichloroacetylene to be explosive when a condenser was used but such explosions could be prevented by the use of an inert gas such as nitrogen, or an excess of trilene. There is no evidence to indicate that reaction B with the production of dichloroacetyl-chloride occurred. The trilene dichloroacetylene mixtures made by ourselves readily decomposed on standing, phosgene and hydrochloric acid being certainly produced. It is evident there are many possibilities from the trilene soda-lime combination and there may be others than these mentioned.

Animal Anæsthetics.—Experimental anæsthetization of rabbits with trilene dichloroacetylene mixtures was vitiated by the presence of *Encephalitozoon cuniculi* in our animals; marked histological changes were seen in the brains of controls as well as the animals treated. However two of those receiving 5% dichloroacetylene on an open mask died—one within twenty-four hours and the other in four days. Both showed signs of acute pulmonary œdema and these lung changes were probably due to phosgene. The mixture in the bottle had exploded several times during the administrations.

Although evident experimentally and its effect noted on animals there was never any

clinical evidence of phosgene in the anæsthetics administered to patients.   Drs. Perry, Milton and Graham, working with Dr. Hunter at the Department for Research in Industrial Medicine, have confirmed Dr. Cox's experiments and plan to investigate the subject further.

CONCLUSION

The virus theory was neither proved nor disproved but all the evidence points to a toxic drug effect following reactions between trilene and soda-lime.

It was realized that trilene could have persisted in the machine or the soda-lime which may have been "rested" for as long as three days.   The use of the contaminated soda-lime at a later date might explain the intervals between the trilene administrations and the anæsthetics which were followed by palsies.

It should be remembered that variations in susceptibility are well known in toxicology. There is no doubt that trilene can combine with soda-lime to form extremely toxic products and any possibility of this combination should be avoided in anæsthetic practice.

BIBLIOGRAPHY

ANDREWES, C. H., and CARMICHAEL, E. A. (1930) *Lancet* (i), 857.
BRAIN, R. T. (1932) *Brit. J. exp. Path.*, **13**, 166.
BROWNING, ETHEL (1937) Toxicity of Industrial Organic Solvents—Summaries of Published Works. London.
DOERR, R., and BERGER, W. (1922) *Schweiz. med. Wschr.*, **52**, 862.
FLEXNER, S., and AMOSS, H. L. (1925) *J. exp. Med.*, **41**, 218.
HARRIS, W. (1937) The Facial Neuralgias. London.
HEWER, C. L. (1943) *Proc. R. Soc. Med.*, **36**, 463.
KEDDIE, F. M., REES, R. B., and EPSTEIN, N. N. (1941) *J. Amer. med. Ass.*, **117**, 1327.
McAULEY, J. (1943) *Brit. med. J.* (ii), 713.
MORTON, H. J. V. (1943) *Brit. med. J.*, (ii), 828.
STUBER, K. (1931) *Arch. Gewerbepath. Gewerbehyg.* (ii), 398.

Mr. C. Langton Hewer, commenting on Dr. McClelland's paper, said that, so far as he knew, in every reported case of nervous sequelæ after closed-circuit anæsthesia, one particular brand of soda-lime had been used which had most undesirable characteristics from the anæsthetist's point of view.   On analysis this soda-lime contained over nine times the caustic soda content which was regarded as optimal.   Furthermore, it was five times as hygroscopic as a good brand in constant use, and after a short time it set into a hard mass which exerted considerable resistance to respiration.   The temperature of the canister also became extremely high (180° F.) and this would naturally accelerate any chemical reaction with an anæsthetic agent.   In Mr. Hewer's opinion it was doubtful if any trouble would have been encountered with trilene using a fresh canister of good soda-lime for each case, and in fact many thousands of administrations had been so given without incident.   At the same time, Dr. McClelland had performed a service in calling attention to the danger of decomposition and it would seem wise to avoid closed-circuits altogether when using trilene.

Electrocardiographic Changes during Trilene Anæsthesia

By C. G. BARNES, M.D., F.R.C.P., and JOHN IVES, M.B., D.A.

INTRODUCTION

THE changes in cardiac rhythm which occur during trilene anæsthesia are regarded by some with alarm whilst others consider them to be of no importance.   There seem to be two reasons for this divergence of opinion.   In the first place the exact nature, and therefore the significance, of these arrhythmias cannot properly be determined unless frequent electrocardiograms (E.C.G.) are recorded throughout the anæsthetic, and up to the present this has been done only in six cases.   Secondly, in the reported cases in which marked arrhythmias occurred there have been other factors—such as intubation—which might themselves be held responsible for the change in rhythm.

Summarizing the findings of various investigators (*see* Bibliography), it appears that marked cardiac disturbances have occurred with trilene when the anæsthesia has been deep, when intubation has been used, and when cyclopropane or adrenaline has been added.   In addition, absorption technique has frequently been employed in these investigations, and it is possible that decomposition products of trilene and soda-lime could have affected the heart.   It is not clear whether light trilene anæsthesia, without these accessory factors, has caused serious arrhythmias.   The object of our investigation, therefore, was to take E.C.G.s throughout operations performed on healthy patients under light trilene anæsthesia, selecting cases which needed no greater depth of anæsthesia than the upper second plane and avoiding the complicating factors of cyclopropane, intubation, use of an absorber, and the application of adrenaline.   In this way the nature and frequency of cardiac arrhythmias due to trilene itself have been determined.

Course of the investigation.—Forty patients have been investigated, 30 males and 10 females. All of these were examined clinically by one of us (C. G. B.) on the day before the operation and a routine 3-lead E.C.G. was taken. Each subject selected for this inquiry was normal clinically and showed a physiological E.C.G. Their ages varied from 10 to 74 years, 33 being between 20 and 60 years of age. In 28 cases the operation performed was herniorrhaphy, the remaining operations being epididymectomy in 4 cases, radical mastectomy in 2, closure of a sinus in 2, for bilateral hallux valgus in 2, and ovarian cystectomy and colostomy each in 1 case. For premedication 30 patients were given omnopon and scopolamine, 9 seconal and scopolamine, and 1 atropine alone. The average duration of anæsthesia was 36 minutes, the shortest being 15 minutes and the longest 95 minutes. The average rate of consumption of trilene was 3½ drachms an hour. The Boyle's machine was used with a nitrous-oxide induction preceding the trilene in every case. Care was taken to avoid anoxæmia but this was not always possible for the anæsthetic was sometimes unsatisfactory and occasionally there was difficulty with the airway. Two patients who showed multi-focal ventricular tachycardia, as described below, developed reflex laryngeal spasm, but anoxæmia alone cannot be held responsible, for the same changes occurred in two other patients without anoxæmia.

Before the anæsthetic started direct contact electrodes were applied to the patients' limbs, and then E.C.G.s were taken at intervals throughout the anæsthetic on lead 2 only—this lead being chosen because any changes occurring in leads 1 or 3 must be reflected in lead 2. The movements of the fibres were watched for a few beats every minute throughout the operation, and a record was taken immediately the slightest change was observed. If no changes were seen a tracing was taken as a routine every five minutes. At the end of the operation, when the patient was still unconscious and the surgeon sewing up, a 3-lead E.C.G. was taken, and a final 3-lead record was obtained in thirty of our patients between three and seven days after the operation, in case any late changes in the cardiographic pattern appeared. In this way nearly four hundred tracings were obtained during this series and any arrhythmia or other change which escaped record must have been very transient. A portable Cambridge electrocardiograph was used throughout the investigation.

Results of the investigation.—Cardiac disturbances during the anæsthetic were noticed clinically in 12 cases, bradycardia and occasional premature contractions being the most common changes. *Pulsus bigeminus* was found in 1 case and 2 others each developed for a short period a rapid and completely irregular pulse. These few arrhythmias were in striking contrast to the large number observed cardiographically, for only 7 of our 40 patients showed no change at all in the E.C.G. during the operation.

Very many varieties of arrhythmia were observed in the E.C.G.s and it was common for a patient to exhibit several of these successively as the anæsthetic continued.

In general, however, these alterations in rhythm fall naturally into two groups. In the first there was a series of changes due probably to increase in vagal tone, and these tended to occur in the first ten or twelve minutes—often in the induction phase of the anæsthetic. We noticed that these changes were more likely to occur in those patients who showed signs suggestive of high vagal tone before operation, in the form of bradycardia and sinus arrhythmia. They consisted of sinus bradycardia (the heart-rate sometimes falling below 40 beats a minute), alteration in the voltage of the P wave with shifting pace-maker, auricular standstill, partial auriculoventricular block, complete auriculoventricular dissociation, and auriculoventricular nodal rhythm—this last being very common and observed in 15 of our patients. The frequency of each of these arrhythmias is shown in the table; they were all transient and disappeared as the anæsthetic continued.

ELECTROCARDIOGRAPHIC CHANGES DURING TRICHLORETHYLENE ANÆSTHESIA

Abnormality						No. of Cases	Per cent.
Total cases	...	...	...			40	100
No abnormality	...	...	...			7	17·5
Sinus bradycardia (under 50)	...	...	...			10	25
Sinus bradycardia (under 40)	...	...	...			4	10
Shifting pace maker	...	...	...			9	22·5
Auricular standstill	...	...	...			1	2·5
A-V nodal rhythm	...	...	...			15	37·5
Prolonged A-V conduction time	...	...	...			2	5
Complete A-V dissociation ...	...	...	...			4	10
Auricular premature contractions	...	...	...			5	12·5
Ventricular premature contractions	...	...	...			16	40
Coupled beats	...	...	...			11	27·5
Multifocal ventricular contractions	...	...	...			6	15
Multifocal ventricular tachycardia	...	...	...			4	10

The second group of arrhythmias tended to occur later, during the lower first or upper second plane, and took the form of ectopic foci initiating premature contractions sometimes in the auricles (in 5 cases), but more often in the ventricles (in 16 cases). At first the ectopic beats occurred quite haphazardly, and from a single focus, but as the anæsthetic proceeded they gave way in 11 patients to alternating ventricular premature contractions causing *pulsus bigeminus*. Shortly after this, in 6 cases, they were followed by multiple ventricular contractions arising from several different foci, and in 4 patients these abnormal beats occurred at a great rate—between 130 and 200 a minute—to give extremely bizarre tracings in the E.C.G. This last arrhythmia is, we believe, important, and we shall refer to it as "multifocal ventricular tachycardia" (figs. 1 and 2).

It must be emphasized that with this arrhythmia the pulse becomes completely irregular and extremely rapid, in fact indistinguishable clinically from auricular fibrillation. It seems probable that the cases of auricular fibrillation observed clinically under trilene anæsthesia have really been examples of this multifocal ventricular tachycardia.

Although we have described two groups of arrhythmia they are not sharply separated one from another with regard to the time at which they occur—we have, for example, observed nodal rhythm late in the anæsthetic, and perhaps more important, ventricular premature contractions during the induction of the anæsthetic.

Throughout this series we have not noticed any significant changes in the R-T interval or in the T waves, and no late changes for which the anæsthetic could be held responsible were seen in the E.C.G.s taken at the end of the operation or in those recorded several days later.

Two patients only showed late changes in the E.C.G.

Case 24 sustained a massive pulmonary embolus due to a deep femoral thrombosis
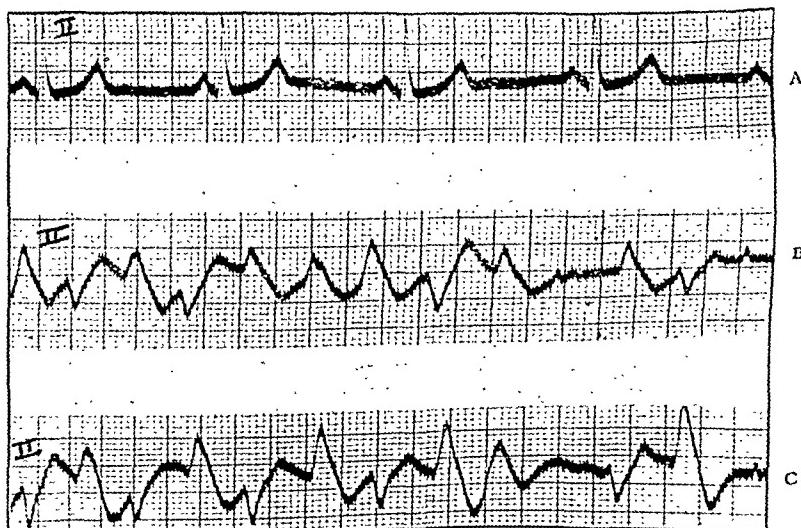
FIG. 1 (*Case* 5).—A, Sinus rhythm before anæsthesia. Multifocal ventricular tachycardia, B at 19 minutes, and C at 20 minutes, after start of anæsthetic.

a week after the operation; his E.C.G. at that time showed the characteristic appearance of acute cor pulmonale.

Case 13 developed pneumonia, pleurisy and pericarditis four days after the operation. His E.C.G. shows inversion of the T wave in all leads, which was almost certainly the result of the pericarditis. This patient has since returned for another operation. He was again given trilene and showed no post-operative change at all in the E.C.G.

DISCUSSION

Are any of these cardiographic changes of importance or are they merely curiosities which although interesting to the physician can be safely ignored by the practising anæsthetist? If they are potentially dangerous, do they occur more frequently with trilene than with other anæsthetics?

The first group of arrhythmias due possibly to increase in vagal tone have been described with practically every type of inhalation anæsthetic, including chloroform, ether, cyclopropane, trilene, ethyl chloride and gas-and-oxygen. They are always transient, and as some of them, such as nodal rhythm and delayed auriculoventricular conduction, are not to be recognized without mechanical aids they must be far more frequent than anæsthetists generally realize. There is no reason on general medical grounds to believe them dangerous, and the extremely low cardiac mortality rate with anæsthetics such as ether and gas-and-oxygen confirms this impression. This also applies to simple premature contractions whether they be auricular or ventricular.

More attention must be paid, however, to the multifocal ventricular tachycardia observed in four of our patients, that is in 10% of our series. We have not found this arrhythmia demonstrated by E.C.G. under any anæsthetic except chloroform, cyclopropane and trilene, although a case was recorded by Geiger (1943) after inhalation of carbon tetrachloride.

Levy showed this type of arrhythmia in cats under light chloroform anæsthesia, whilst clinically Hill (1932 *a* and *b*) showed multifocal ventricular premature contractions in seven out of eighteen patients in whom anæsthesia was induced with chloroform. Kurtz, Bennett and Shapiro (1936) recorded multifocal ventricular tachycardia in 4 out of 41
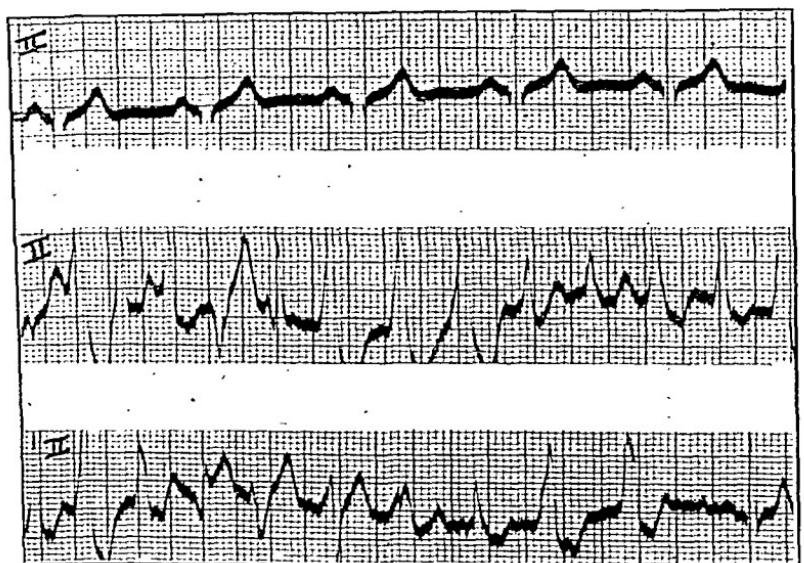
FIG. 2 (*Case* 34).—A, Sinus rhythm before anæsthesia. Multifocal ventricular tachycardia, B at 13 minutes and C at 16 minutes, after start of anæsthetic.

cases of cyclopropane anæsthesia—an incidence practically identical with that in our own series under trilene. Waters *et al.* (1943) found the same arrhythmia under trilene anæsthesia but their patients were known to have myocardial degeneration before operation. The similarity of the cardiographic patterns between our cases and those published by Hill and by Kurtz and his colleagues is most striking.

Although occasional premature contractions of any type can be ignored clinically as having in themselves no prognostic significance when they arise from a single focus, we know that multifocal ventricular premature contractions, particularly if they occur when the heart is rapid, are much more likely to be associated with myocardial damage. The well-known work of Levy and Lewis (1911) and Levy (1913), showed that fatal ventricular fibrillation in cats under chloroform anæsthesia was invariably preceded by multifocal ventricular tachycardia, the change from the one arrhythmia to the other being precipitated by injection of adrenaline, although, of course, not every case of ventricular tachycardia went on to fibrillation.

One might suppose, therefore, that this multifocal ventricular tachycardia is potentially dangerous, but against this view must be set the fact that only one death has been reported from heart failure under trilene anæsthesia (Haworth and Duff, 1943) although

there have been many under chloroform and some under cyclopropane (Waters and Gillespie, 1944). We must remember, however, as Geiger (1943) has pointed out, that in the industrial field sudden death has occurred in workers with pure trichlorethylene, and at autopsy no satisfactory organic cause for death has been demonstrated.

It is possible to correlate these apparent contradictions when one remembers that the arrhythmia occurs early in chloroform anæsthesia, during induction, when the out-pouring of adrenaline as a result of the patient's fear or struggling might be expected to convert it into fatal ventricular fibrillation. Anæsthesia was not induced from the outset with trilene in our cases so we cannot tell whether the same thing might not happen with this anæsthetic if it were. The arrhythmia occurred late and by this time the patient was no longer struggling and the early part of the induction with gas-and-oxygen was usually quiet and uneventful.

Our results suggest that the frequency of multifocal ventricular tachycardia under trilene anæsthesia constitutes a potential danger, particularly if adrenaline is used during the anæsthetic. We therefore find ourselves in agreement with Hunter's conclusion (1944) that trilene should not be used as a routine adjuvant to gas and oxygen.

BIBLIOGRAPHY

GEIGER, A. J. (1943) *J. Amer. Med. Ass.*, **123**, 141.
GORDON, R. A., and SHACKLETON, R. P. W. (1943) *Brit. med. J.* (i) 380.
HAWORTH, J., and DUFF, A. (1943) *Brit. med. J.* (i), 381.
HEWER, C. L. (1942) *Proc. R. Soc. Med.*, **35**, 463.
—— (1943) *Proc. R. Soc. Med.*, **36**, 463.
HILL, I. G. W. (1932a) *Edinburgh Med. J.*, **39**, 533.
—— (1932b) *Lancet* (i), 1139.
HUNTER, A. R. (1944) *Lancet* (i), 308.
JOHNSON, E. E. (1944) *Lancet* (i), 357.
KURTZ, C. M., BENNETT, J. H., and SHAPIRO, H. H. (1936) *J. Amer. Med. Ass.*, **106**, 434.
LEVY, A. G. (1913) *Heart*, **5**, 299.
——, and LEWIS, T. (1911) *Heart*, **3**, 99.
LLOYD WILLIAMS, K. G., and HEWSPEAR, D. (1942) *Brit. med. J.* (ii), 170.
REID, L. C., and BRACE, D. E. (1940) *Surg. Gynæc. and Obstet.* (ii), **70**, 157.
WATERS, R. M., and GILLESPIE, N. A. (1944) *Anesthesiology*, **5**, 113.
——, ORTH, O. S., and GILLESPIE, N. A. (1943) *Anesthesiology*, **4**, 1.

Mr. C. Langton Hewer, referring to the paper by Dr. Barnes and Dr. Ives, said he rather doubted the value of electrocardiograms in assessing the practical value of an anæsthetic drug. He believed that all the abnormal tracings described had also been observed during cyclopropane narcosis. Certainly arrhythmias of all kinds were common with the latter drug but no ill-effects seemed to occur. Mr. Hewer suggested that two practical questions arose: (1) Did the arrhythmias ever persist after anæsthesia? and (2) Did they ever culminate in primary cardiac failure, e.g. from ventricular fibrillation? So far as he knew, no permanent cardiac changes had been described and one or possibly two cases of primary cardiac failure. As the total number of trichlorethylene administrations in this country alone must well exceed half a million, the incidence is extremely low for a general anæsthetic, in marked contrast to chloroform. In over three years' continuous experience with trilene, Mr. Hewer had never seen any serious circulatory changes which were attributable to the drug. It was by no means a perfect anæsthetic but it was extremely useful for the induction and maintenance of light planes of narcosis and as a general analgesic.

JOINT DISCUSSION No. 4

Section of Surgery with Section of Anæsthetics

Chairman—Sir James Walton, K.C.V.O., M.S.

(President of Section of Surgery)

[*April* 5, 1944]

DISCUSSION ON ANÆSTHESIA AND ANALGESIA IN ABDOMINAL OPERATIONS

Surgeon Rear-Admiral G. Gordon-Taylor [*Abridged and Introduction omitted*]: Inasmuch as the patient's survival is the most important consideration for both surgeon and anæsthetist, the operative mortality attending a given surgical procedure carried out under varying types of anæsthesia might be thought to furnish an index of some value in appraising any method of abdominal anæsthesia; but operative mortality in abdominal surgery depends on many factors apart from the administration of an anæsthetic. The following circumstances, for example, may also contribute to the result—the extent of the pathological lesion, its duration and the resultant constitutional effects therefrom; the skill and judgment of the surgeon, his timidity or alternatively his boldness; the wise employment of pre-operative means making the patient "safe for surgery"; the skilful use of post-operative measures; everything that constitutes the patient a "good" or "bad surgical risk"; the environment of the operation; all these contribute to success or failure. Operative mortality may not be the whole answer to aid us in our quest for the best form of abdominal anæsthesia, but *safety, absolute safety* of the method is at least a *prime consideration*.

"Balanced anæsthesia"! perhaps a modern term for an old concept and practice, with this difference, as I see it, that pharmacological admixture has to-day run riot in a reckless orgy. Forty years have elapsed since the great American surgeon, George Crile, first toyed with his kinetic theory of shock and evolved the shockless operation through anoci-association. For my part, I have counted myself an adherent of the Crile school for 30 years, and my anæsthetic colleagues have been my loyal coadjutors and acolytes in our operative practice.

Tumours of the abdominal wall.—The removal of a malignant or semi-malignant tumour of the abdominal wall, always a rather carnivorous procedure, often involving the sacrifice of considerable portions of the parietes surrounded by incisions of irregular pattern, may be productive of the most severe shock. Such operations as the ablation of a large desmoid tumour or a visceral carcinoma implicating the abdominal musculature call for the employment of regional anæsthesia in addition to inhalation or intravenous methods.

Furthermore, the loyal and wise co-operation of the anæsthetist cannot be overrated in such an operation as the *Interinnomino-Abdominal-amputation* ("hind-quarter" amputation) where part of the bony and muscular wall of the belly as well as the whole of the lower limb are removed; we have had 17 cases of this operation with 12

there have been many under chloroform and some under cyclopropane (Waters and Gillespie, 1944). We must remember, however, as Geiger (1943) has pointed out, that in the industrial field sudden death has occurred in workers with pure trichlorethylene, and at autopsy no satisfactory organic cause for death has been demonstrated.

It is possible to correlate these apparent contradictions when one remembers that the arrhythmia occurs early in chloroform anæsthesia, during induction, when the outpouring of adrenaline as a result of the patient's fear or struggling might be expected to convert it into fatal ventricular fibrillation. Anæsthesia was not induced from the outset with trilene in our cases so we cannot tell whether the same thing might not happen with this anæsthetic if it were. The arrhythmia occurred late and by this time the patient was no longer struggling and the early part of the induction with gas-and-oxygen was usually quiet and uneventful.

Our results suggest that the frequency of multifocal ventricular tachycardia under trilene anæsthesia constitutes a potential danger, particularly if adrenaline is used during the anæsthetic. We therefore find ourselves in agreement with Hunter's conclusion (1944) that trilene should not be used as a routine adjuvant to gas and oxygen.

BIBLIOGRAPHY

GEIGER, A. J. (1943) *J. Amer. Med. Ass.*, **123**, 141.
GORDON, R. A., and SHACKLETON, R. P. W. (1943) *Brit. med. J.* (i) 380.
HAWORTH, J., and DUFF, A. (1943) *Brit. med. J.* (i), 381.
HEWER, C. L. (1942) *Proc. R. Soc. Med.*, **35**, 463.
——— (1943) *Proc. R. Soc. Med.*, **36**, 463.
HILL, I. G. W. (1932a) *Edinburgh Med. J.*, **39**, 533.
——— (1932b) *Lancet* (i), 1139.
HUNTER, A. R. (1944) *Lancet* (i), 308.
JOHNSON, E. E. (1944) *Lancet* (i), 357.
KURTZ, C. M., BENNETT, J. H., and SHAPIRO, H. H. (1936) *J. Amer. Med. Ass.*, **106**, 434.
LEVY, A. G. (1913) *Heart*, **5**, 299.
———, and LEWIS, T. (1911) *Heart*, **3**, 99.
LLOYD WILLIAMS, K. G., and HEWSPEAR, D. (1942) *Brit. med. J.* (ii), 170.
REID, L. C., and BRACE, D. E. (1940) *Surg. Gynæc. and Obstet.* (ii), **70**, 157.
WATERS, R. M., and GILLESPIE, N. A. (1944) *Anesthesiology*, **5**, 113.
———, ORTH, O. S., and GILLESPIE, N. A. (1943) *Anesthesiology*, **4**, 1.

Mr. C. Langton Hewer, referring to the paper by Dr. Barnes and Dr. Ives, said he rather doubted the value of electrocardiograms in assessing the practical value of an anæsthetic drug. He believed that all the abnormal tracings described had also been observed during cyclopropane narcosis. Certainly arrhythmias of all kinds were common with the latter drug but no ill-effects seemed to occur. Mr. Hewer suggested that two practical questions arose: (1) Did the arrhythmias ever persist after anæsthesia? and (2) Did they ever culminate in primary cardiac failure, e.g. from ventricular fibrillation? So far as he knew, no permanent cardiac changes had been described and one or possibly two cases of primary cardiac failure. As the total number of trichlorethylene administrations in this country alone must well exceed half a million, the incidence is extremely low for a general anæsthetic, in marked contrast to chloroform. In over three years' continuous experience with trilene, Mr. Hewer had never seen any serious circulatory changes which were attributable to the drug. It was by no means a perfect anæsthetic but it was extremely useful for the induction and maintenance of light planes of narcosis and as a general analgesic.

rare chance occur, was readily recovered from in those who had not been subjected to drenching of the respiratory passages with ether.

Our regional anæsthesia has been secured by the rectus field block. I am not prepared to deny that the thoracic block four fingers from the spinous processes just outside the erector spinæ may be a better method; the pararectal route which we have used for so long has satisfied me. Perhaps the relaxation of the abdominal wall is better with the thoracic infiltration, but the action of a larger number of muscles of respiration is interfered with—e.g. the intercostals, part of the diaphragm, the abdominal obliques, &c.

I have also remained loyal to novocain. For the slow operator, percaine may be invaluable, as may decicain (amethocaine hydrochloride or anethaine). On the other hand mixtures of these drugs may be employed so as to ensure quick action and prolonged duration.

. The degree of relaxation obtained by the use of the pararectal and splanchnic block is such that *I have never used a retractor for any gastric operation.* The thought of an automatic retractor evokes a shudder; "every pull is a pain". Where a high gastrectomy is demanded, the infiltration of the diaphragm facilitates surgery.

I am not prepared to claim a relationship between the absence of vomiting and the regional method of anæsthesia, but it is indisputable that in our cases the ubiquitous forest of masts and plethora of glass amphoræ associated with intravenous fluids and gastric suction almost invariably seen nowadays have been found necessary in a paltry 5% of our cases.

In contradistinction to spinal anæsthesia there is no alarming fall of blood-pressure; the fall of blood-pressure with splanchnic anæsthesia is of smaller degree, requires no added drug to combat the fall and the blood-pressure at the termination of the operation is often more elevated than at the commencement of the procedure, without the aid of any added drug or intravenous fluid.

The great value of regional and splanchnic anæsthesia in the "bad risk" patient should be specially emphasized; in the operative treatment of hæmatemesis from peptic ulcer the importance of this method is inestimable. Should any general narcosis be required in such cases, gas and oxygen is the only form of anæsthesia that should be employed.

I have included several tables setting forth the respective mortality attending the operation of gastrectomy performed for peptic ulcer with various forms of anæsthesia by different surgeons. These figures clearly cannot be fairly weighed against each other; the surgeon who performs gastrectomy at an early stage for every small gastric or duodenal ulcer will obviously boast an enviably low operative mortality; whereas the surgeon who defers operation until the patient has "earned" an operation will have a higher fatality rate. Although for nearly a quarter of a century I have regarded gastrectomy as the appropriate surgical treatment for duodenal ulcer, and though duodenal ulcer is admittedly a much more frequent condition than is gastric ulcer, my gastrectomies for ulcer of the stomach are more than twice as numerous as those for duodenal ulcer. I have always reserved operation for chronic duodenal ulcer for patients with stenosis, with recurrent hæmorrhage, with a huge massive crater-form ulcer or those whose means of livelihood is being constantly interrupted and jeopardized by recurrent crippling illness. It will be obvious that my material will not yield such good immediate operative results as attend the impetuous gastrectomist.

Scrutiny often engenders surprise and regret that mortality is found to be higher than had been anticipated, and I confess to a sense of disappointment that my operative mortality for over twenty-four years has amounted to 6·5%; although there is this consolation that in the last six years the mortality-rate has fallen to only 2·7%.

It is probably fair to say that the younger generation of surgeons is finding a short cut to safe gastrectomy for ulcer through the employment of regional and splanchnic anæsthesia, and such can within a few years challenge the results of their elders which have been secured on the hard road of long experience.

Perhaps insufficient attention has been drawn to the *time factor in operation;* the longer a patient is immobilized upon the table under any form of general or local anæsthesia, the more likely is he to develop pulmonary complications. The depth of anæsthesia, and the duration of time under pre-medication and post-operative drugs also markedly contribute to the immobilization of the pulmonary bases, sluggish venous return, anoxia, &c. (Gillies).

recoveries. A *unilateral* intra-arachnoid spinal block with stovaine or percaine (nupercaine), along with gas, oxygen and ether has been the method almost exclusively employed. The sacral nerves are also blocked with novocain immediately before they are cut; ligature of the posterior division of the internal iliac artery at as early a stage as possible, and the most careful changing of the posture of the patient during the progress of this colossal operation appear valuable aids towards promoting the success of the undertaking.

The abdominal viscera.—The fate of the "abdominal" patient is everywhere more intimately related to the activities of the surgeon than to the ministrations of the anæsthetist; but there are certain regions of the belly where choice of anæsthetic does appear to influence the result more powerfully than others.

Except in complicated cases of *cholelithiasis*, e.g. the severe bronchitic or the jaundiced patient, the anæsthetic does not seem greatly to influence the result of cholecystectomy. Ten years once elapsed in my own experience without the loss of a simple cholecystectomy; the use of the Kocher incision, the experience and rapidity of the surgeon count for much. On the other hand, the jaundiced patient requires gas and oxygen, or spinal anæsthesia, and in such cases as the repair of disastrous damage to the main hepatic duct inflicted during maladroit cholecystectomy, where a prolonged operation seems possible or probable, spinal anæsthesia along with gas and oxygen may be the best combination. The greatly lowered mortality is due as much to preliminary treatment with vitamin-K and bile salts, and the employment of intravenous glucose and certain of the amino-acids, as to any choice of anæsthesia.

Surgical technique plays a more important rôle than anæsthesia in the successful removal of an unobstructed *cancer of the colon*. On the other hand, "blind cæcostomy" is most safely performed under regional anæsthesia, and this anæsthetic is ideal for the operative relief of a strangulated hernia.

Cancer of Rectum.—Appropriate preliminary medication, 1/1,500 percaine spinal anæsthesia, along with gas and oxygen appears to be the method of election.

For bladder and prostatic surgery a low spinal anæsthetic, a pararectal regional block, and gas and oxygen are probably the best combination.

In the "bad surgical risk", the *kidney* can be satisfactorily dealt with under a paravertebral block or high spinal anæsthesia, the former being probably the better method.

The *upper abdomen* is perhaps the chief tilting ground for champions of rival methods of anæsthesia, and doubtless much of the interest in this discussion will centre round the question of *anæsthesia in gastric surgery*.

Gastrectomy for cancer.—The mortality of this operation is hardly to be ascribed to the particular type of anæsthesia employed, although I have seen Finsterer succeed in the removal of a huge cancer of the stomach under regional and splanchnic anæsthesia without blood transfusion, where I could scarce have envisaged a favourable issue under any other form of anæsthetic. The percentage of operative deaths in the hands of those who have dealt with a large number of cases of gastric cancer is depressingly high, but this is no reflexion on the anæsthesia or upon the surgeon. Yudin admits a mortality of 30% for total gastrectomy for cancer, which is performed under spinal anæsthesia, and his series embraces no fewer than 100 cases.

The surgery of peptic ulcer.—I have been using regional and splanchnic anæsthesia for upwards of 20 years for gastro-duodenal resection for ulcer. The solar plexus and splanchnics were in the earliest years injected from the loins; our experience of the Kappis technique was reported by Raymond Apperly in this very room in 1925; but for the last nineteen years the solar plexus has been approached trans-abdominally by the Braun technique. Greater accuracy has undoubtedly been obtained thereby.

In a certain percentage of the cases of the past twenty-two years reliance has been placed entirely on regional and splanchnic analgesia, but in far the greater number the very lightest form of general narcosis has been added, ether and chloroform being used in the minutest amounts; it has been a point of honour with the anæsthetist that the patient be kept under the very slightest depth of anæsthesia, so that he can readily respond to any question addressed to him. Gas and oxygen might perhaps have been used more frequently, but I have personally never been impressed with prolonged operations under a "nosebag" employed as a routine measure.

I have *never used spinal anæsthesia for any gastric operation;* I may have lacked the complete relaxation which this ensures, but I have had little desire to experiment personally with new methods of anæsthesia when satisfaction was felt with the old. Chest complications have been rare; long before the sulphapyridine era pneumonia, should this by

In many of H.M. Ships, especially those with only one medical officer, e.g. Rescue Ships attached to convoys, the Oxford Ether Vaporizer has proved invaluable; its popularity is attested by increasingly frequent requests to the medical department of the Admiralty for this machine.

The possibility of a sudden order to "abandon ship" must always be borne in mind when choice of anæsthetic afloat is under consideration; some medical officers with experiences of air-bombardment of ships are even nervous about morphia and would only permit the short-duration intravenous forms of anæsthesia.

For acute abdominal conditions, such as acute appendicitis, strangulated hernia, intestinal obstruction, perforated peptic ulcer, &c., afloat, Woolmer [18] recommends spinal analgesia, but such a choice surely demands a very experienced and expert anæsthetist.

Despite modern criticism, there is something to be said for chloroform, at least in careful Scottish hands! It is simple, compact, non-inflammable, and has been included in the armamentarium of L.S.T. ships employed to transport casualties in the recent Normandy invasion. Some comfort for the timid may be found in the statement that sulphanilamide tends to protect the liver against the toxic effects of chloroform!

Abdominal anæsthesia for gunshot wounds in the field.—I find no evidence to make me retract the slogan that I have so often used in relation to the early surgery of the abdominal wounds of war: "spinal anæsthesia is certain euthanasia." Brigadier Ashley Daly and my many friends in "forward surgical units" in the Mediterranean field of operations (Truscott, Till, Handley, Blackburn, Law, Louden, &c.) all eulogize ether, with or without gas and oxygen. With present-day mobility of armies there may be difficulties about the transportation of gas and oxygen, but twenty-five years ago no surgeon on the British Front had results approaching those of D. E. Taylor, who employed regional anæsthesia and also enjoyed the advantage of the services of Geoffrey Marshall, who did so much to instruct the anæsthetists of the Casualty Clearing Zone in the use of gas and oxygen. I have no doubt that *regional anæsthesia along with gas and oxygen is the best method of all.*

In many zones of the belly choice of anæsthetic seems to count less in achieving success than the quality and judgment of the surgeon; to these problems I have made scanty reference. My views and practice, however, are not too crystallized to obscure my vision, and I am full of enthusiasm for a still greater future in the surgery of the belly to be won by the combined effort of surgeon and anæsthetist in the years to come. Every work is not only an end, but also the means—a means of accomplishing some day hence a work that shall be higher and more noble still.

When the riband of the history of anæsthesia is finally unrolled, through it will be found running the scarlet thread of British and American endeavour, bourgeoning here and there into a wider and more vivid strand through the work of some specially illustrious contributor—Davy, Hickman, Morton, Simpson, Pirogov, Gwathmey, Meltzer and Auer, Robert Kelly, the surgeon, and many more.

SUMMARY

The best form of abdominal anæsthesia will always be achieved by the employment of the appropriate type of anæsthetic by the most skilful anæsthetist for the appropriate patient in the particular environment.

(1) The value of regional and splanchnic anæsthesia in abdominal surgery is indubitable.

(2) Its special worth lies in the operative surgery of that group of cases which constitute the "bad surgical risk".

Finally the value of these combined discussions is great, and some who participate and some who listen may perchance hear those lines of Terence ringing in their ears:

Quanti est sapere! Nunquam accedo ad te,
quin abs te abeam doctior.

(Terence, *Eunuchus* V.1.XXI).

BIBLIOGRAPHY

1 MOYNIHAN, Lord (1921) Essays on Surgical Subjects, p. 109. Philadelphia and London.
2 PANNETT, C. A. (1935) *Surg. Gynec. Obstet.*, 67, 495.
3 GRAHAM, R. ROSCOE- (1938) *Surg. Gynec. Obstet.*, 66, 269.
4 MAINGOT, RODNEY (1940) Abdominal Operations, vol. i, p. 317. New York and London.
5 LAKE, NORMAN (1938) *Lancet* (ii), 241.
6 YUDIN, S. S. Personal communication and in the press.
7 LAHEY, FRANK, and MARSHALL, S. E. (1943) *Surg. Gynec. Obstet.*, 76, 641.

INHALATION ANÆSTHESIA.

References			Percentage mortality
Moynihan [1]	Over 100 gastric ulcers		1·6
Pannett [2] (1938)	Gastro-duodenal resection		
	Billroth I.		
	{ Duodenal ulcer, 42	3 deaths	7
	{ Gastric ulcer, 28	1 death	3·6
	Billroth II.		
	{ Duodenal ulcer, 116	1 death	0·86
	{ Gastric ulcer, 66	4 deaths	6
Roscoe-Graham [3] (1938) (Toronto)	Duodenal ulcer, 131	3 deaths	2·5
	Gastric ulcer, 33	5 deaths	15
R. Maingot [4] (1942)			4

HIGH SPINAL ANÆSTHESIA.

			Percentage mortality
Norman Lake [5] (1938)	Gastrectomy (ulcer) 269	27 *deaths*	10

(N.B.—Chest complications were responsible for 35 per cent. of fatal cases.)

Yudin [6] (1943)	Gastro-duodenal resections for *acute perforated ulcer*, 331	21 deaths	6·3

(N.B.—For bad cases of perforation Yudin employs local anæsthesia or local+ether.)

	For *chronic ulcer*		5
Frank Lahey [7] (1943)	Gastrectomy for ulcer, 251	8 deaths	3·2

REGIONAL AND SPLANCHNIC ANALGESIA

J. Duval [8]	Gastrectomies (ulcer), 125	0 deaths	0
Prof. Haas [9] (Munich)	Gastrectomies (ulcer), 250	0 deaths	0
H.W.L.Molesworth [10]	Gastrectomies (ulcer), 119	3 deaths	2·5
W. J. Ferguson [11] (West Middlesex Hospital)	Gastrectomies (ulcer), 202	7 deaths	3·5
Norman Tanner [12] (St. James's Hospital, Balham)	Just under 100 Gastrectomies (1939 to May 1941) (ulcer)	4 deaths	4
	Gastrectomies (ulcer), 120 (May 1941 to end of 1942) (Using prophylactic sulphapyridine)	1 death	0·8
Hans Finsterer [13]	Over 2,000 cases		from 2·7-3·5
Haberer [14]			5
Bastianelli [15]	Gastrectomies (ulcer), 137		5
Doberer [16] (Linz)	Resections for ulcer, 208 (1930-36)		5·53
W. H. Ogilvie [17] (1935)	Gastric ulcer, 50 gastrectomies	3 deaths	6
	Duodenal ulcer, 15 gastrectomies	0 deaths	0
	{ Gastro-jejunal ulcer, 17 gastrectomies	2 deaths	12
	{ Gastro-jejuno-colic fistula 82 gastrectomies	5 deaths	6
Gordon-Taylor (1920-1944)	{ Gastric ulcer, gastrectomies (including hæmorrhages, gastro-jejunal ulcer and gastro-jejuno-colic fistula) 541	41 deaths	7·6
	{ Duodenal ulcer gastrectomies 253	11 deaths	4·3
	794	52	6·5
Gordon-Taylor (1938-1944)	Gastrectomies 148 (ulcer of all types)	4	2·7

The *abdominal injuries* operated upon in *H.M. Ships* have been scanty: this remark does not of course apply to Hospital Ships who carry a skilled medical staff and modern apparatus.

A marked contrast in the recovery rate of a group of patients with "immersion blast" of the abdomen operated upon in an American hospital ship and disembarked next day, and patients retained afloat for twenty-four hours and operated upon in a hospital ashore twenty-four hours after the incident, whose subsequent evacuation was delayed, affords further proof of the *importance of the retention of the abdominal casualty after operation*, if a successful issue is to be attained. The possibility of pulmonary involvement must also be remembered in cases of "immersion blast," and ether is best avoided. Some form of intravenous anæsthesia combined with gas and oxygen or regional anæsthesia alone seems the appropriate anæsthetic for such cases.

original method of Howard Jones, that of Etherington Wilson, and the technique which I described in 1938 (*Lancet*, July 30, p. 241).

There is no need here to enter into a discussion of the pros and cons of these methods, that has already been done elsewhere, it is sufficient to state that in practice all have proved reasonably satisfactory and safe, such differences as exist are concerned with small factors of relative safety, precision of control, reliability and so on. I shall therefore only describe the method which I now use for, say, a gastrectomy, as good a test as any of a satisfactory anæsthetic from the surgeon's point of view.

The patient, otherwise suitably prepared for the operation, is given a preliminary injection of morphia, gr. ¼, and often, to diminish the unopposed vagal action, a small dose of atropine. On the operating table he is laid prone; after a glance at the curvature of the dorsal spine pillows are so placed under the chest, and the table is so manipulated, that the 7th dorsal spinous process forms the crest of the gently curving back. Observation of this is facilitated by sighting the spinal curve against some horizontal line or object on the wall of the theatre. I find that a black line painted on the wall at a suitable level is of great help for this purpose. The 2/3 lumbar spinous interspace is now identified and the skin and interspinous ligament infiltrated with a little of the solution through a very fine hypodermic needle. The fine bore stainless steel spinal needle, which may with some advantage have a lateral rather than a terminal aperture, is now passed in vertically, deliberately and slowly. Its emergence from the deep surface of the interspinous ligament is easily felt; the next object the point of the needle is felt to penetrate is the dura. In most cases a slow flow of cerebrospinal fluid immediately passes up the vertical needle, but when the intrathecal pressure is very low the fluid may be forced up by asking the patient to cough or by pressing on the jugular veins. The needle is then slightly pushed on and rotated to determine that its point is quite free of arachnoid. If a needle with a lateral aperture is used this should be directed towards the head. It is necessary here to interpose that the needle should be kept keen by an occasional touch on an Arkansas slip, and that the bevel at the end should be a very abrupt one, otherwise the penetration of the dural wall may not be felt. A 10 c.c. syringe containing the previously warmed solution is now carefully attached to the needle and the solution injected very slowly. The idea underlying slow injection is to avoid excessive turbulence at the point which causes rapid mixing with the cerebrospinal fluid, and to enable the solution to trickle up the posterior compartment of the dural sheath to its highest level. The rate should be roughly not greater than 3·0 c.c. per minute. After the injection is completed the needle is held in situ for a further minute so that any leakage on withdrawal will be chiefly cerebrospinal fluid and not anæsthetic. The patient remains steadily in the same position for ten minutes, he is then turned on his back with a slight head down tilt to the table (5 degrees to 10 degrees is sufficient). The operation may immediately begin.

The following points in the technique deserve special attention: (*a*) All syringes and needles must be carefully preserved from any contact with alkali (bicarbonate, &c.) which otherwise precipitates out the percaine. The ampoules in which the solution is issued are made of hard Jena glass for this reason. As an extra precaution the syringe may be washed through with a little of the solution, there being enough in the ampoule to allow of 2 to 3 c.c. being used for this purpose. (*b*) The solution must be warmed before use. This need not be very accurately controlled since slight differences of temperature both above and below that of the body are adjusted during the slow passage of the solution through some 2½ in. of very narrow needle embedded in the tissues, but the initial difference must not be too great, especially on the cold side. (*c*) All the manœuvres should be performed slowly and deliberately.

The quantities to be used are about half those necessary with the Howard Jones technique, thus a gastrectomy may be performed on a small woman with as little as 6·0 c.c. (i.e. 4 mg. percaine), while in a tall man 9·0 c.c. may be required. The standard solution in use is 1/1,500 with added salts to bring the specific gravity at 15·5 C. to 1·0035.

The duration of the anæsthesia obviously depends upon the level under consideration, being greatest in the lower dorsal and upper lumbar regions, where it may last for more than three hours. In the upper abdomen anæsthesia can be relied upon for 1¼ hours. I have recently been using a 1/1,000 solution with great satisfaction, the length of the anæsthesia being extended to 1½ hours with this strength.

The factors controlling the distribution of the anæsthetic in the theca are very complicated, it is impossible to predict theoretically what will happen. Observations, however, appear to indicate that the following account is not far from the truth. The

8 DUVAL, J. (1938) *Clinique Paris*, 33, 35
9 HAAS, Professor. Personal communication.
10 MOLESWORTH, H. W. L. Personal communication.
11 FERGUSON, W. J. Personal communication.
12 TANNER, N. (1943) *Brit. med. J.* (i), 563.
13 FINSTERER, H. *Loc. mult.*
14 HABERER. Quoted by Rodney Maingot (*vide supra*).
15 BASTIANELLI. Quoted by Rodney Maingot (*q.v.*).
16 DOBERER, J. (1937) *Wien. Klin. Wschr.*, 50, 590.
17 OGILVIE, W. H. (1935) *Lancet* (i), 419.
18 WOOLMER, R. (1942) "Anæsthetics Afloat ", p. 99, London.

Mr. Norman Lake : Reduced to the final analysis the reasons for the use of anæsthetics are twofold, first to prevent the patient feeling pain, secondly to enable the surgeon to perform the operation with facility and without interference to his various manœuvres by the movements or rigidity of the patient. In his laudable desire to achieve the first aim, safely and pleasantly, the modern anæsthetist has not infrequently overlooked the fact that the other is equally important. Surgeons appreciated to the full, in the early days of anæsthesia, that its advent would enable them to perform operations of a character that would be technically impossible without complete freedom of action, and that this aspect was if anything more important than the mere abolition of pain, however necessary and desirable this latter might be.

It is an interesting observation that many post-operative complications and sequelæ laid at the door of the surgeon are, when carefully assessed, found to be related to the anæsthesia rather than to the surgery. Examination of one or two of these will illustrate this point and be time well spent. Chest complications after upper abdominal operations were, many years ago, uniformly attributed to the direct effect of the anæsthetic upon the respiratory passages, but, when later it was shown that a lung collapse was a frequent precursor of the more serious inflammatory lesions, the anæsthetic was exonerated and the blame fell upon the shoulders of the surgeon. It was his rough handling of the viscera and extensive exposure of the abdominal contents which led to the collapse, the anæsthetist was very much inclined to wash his hands of the whole thing. It seems to me however that his responsibility is as great as ever for we must inquire why the rough handling was necessary or the exposure prolonged. There are undoubtedly many answers to this question, but other things being equal it is abundantly clear that an unsatisfactory anæsthetic with a rigid abdominal wall and irregular large respiratory excursions may be the most important factor necessitating those manœuvres which are summed up in the expression rough handling. Yet other examples are the later sequelæ, hernia and adhesions. These are particularly likely to occur, apart from the incidence of infection (truly the surgeon's responsibility), when the closure of the abdominal wall becomes a struggle between the needle and the patient's muscles and tissues. I feel sure that every surgeon will agree with this statement. A neatly sutured and undamaged abdominal wall, with good peritoneal apposition, is unlikely to produce the adhesions which all too frequently cause pain and even obstruction subsequently.

My point is that these unfortunate complications are as often due to unsatisfactory anæsthetization as to any defect of surgical technique or lack of skill and it is time that this was more widely admitted.

For abdominal surgery, therefore, and especially that on the upper abdomen emphasis should, I believe, be laid upon the second requirement of anæsthesia, namely the facility afforded to the surgeon to enable him to carry out the operation without the necessity of "rough handling".

It was in this frame of mind that, some fifteen years ago, I was introduced by the late Dr. Howard Jones, to the possibilities of high spinal anæsthesia with light percaine (now nupercaine) solutions. The synthesis of percaine placed in our hands one of the most powerfully anæsthetic substances known, so potent that dilutions of 1/1,000 to 1/2,000 would produce adequate local, regional and spinal anæsthesia. The great virtue of this power lay in the fact that effective solutions had a primary specific gravity less than that of the cerebrospinal fluid, whereas all the materials used up to that time, in effective solutions of 1/100, were initially heavier than that fluid, and were often made still heavier by the addition of glucose, &c., to gain greater gravitational control of the distribution of the solution in the theca; with the same aim other solutions were levitated by the addition of considerable amounts of alcohol (e.g. Kirschner's solution). As simplicity both of technique and of the solution is always desirable, dilute percaine, with the addition only of such salts as would render the solution reasonably isotonic, appeared to meet all requirements and the results of trials showed that it was a highly satisfactory chemical for use in great dilutions for high abdominal anæsthesia. Several different techniques for its administration have been described of which the most used are the

patient under a spinal anæsthetic may refer sensations to his abdominal wall in the same way than an amputee feels his phantom limb, so that it is common experience for a patient to explain that he can still feel quite well while the surgeon makes an extensive incision which entirely fails to attract any attention.

The final point to be mentioned is the psychological aspect. There is no denying that the performance of an extensive operation under this form of anæsthesia is somewhat of an ordeal for the patient, yet I have been very impressed by the large percentage who, when offered gas and oxygen after the operation has been started, reply that they would rather carry on without it. In the last 100 cases, for instance, supplementary general anæsthetics were used in 24, and of these a considerable number were given at the instigation of the surgeon, not because the patients wished it. The preliminary morphia of course helps, but more important is the proper psychological atmosphere in the theatre, and this must be the constant concern of the administrator.

One disadvantage of spinal anæsthesia, especially noticeable in a teaching hospital, is that talk about the operation or the case must be very guarded and scanty.

Nervous sequelæ have not been frequent in the present series. Headaches lasting more than a day or two have been rare, one VIth nerve palsy had not completely recovered at the end of six months, urinary disturbances have been trifling.

Because it avoids, or minimizes, those difficulties and sequelæ of which I spoke at the beginning, I believe that the advantages of high spinal anæsthesia outweigh by far such disadvantages as have been mentioned; I have therefore used it routinely over many years for all gastrectomy and similar operations with increasing satisfaction as time goes on.

Mr. Frankis Evans: Anæsthesia in abdominal surgery must be considered essentially in terms of relaxation. Abdominal relaxation may be obtained in many ways—by inhalation anæsthesia, intravenous anæsthesia, spinal analgesia and regional analgesia. either as a field block of the abdominal wall or as a posterior intercostal block.

Of the inhalation anæsthetics, what has the anæsthetist to choose from? Ether, chloroform, trilene and cyclopropane.

Ether has served us well in the past, but pulmonary complications have been frequent and it is an irritant. 65% to 72% of patients are said to vomit following ether. The chesty patient does not do well on ether. Ether *is* an irritant. It has been shown however, that pulmonary complications follow high spinal and regional analgesia and they even occur after cyclopropane which is non-irritant. Even admitting all that, I still feel that it is wrong to give ether to a chronic bronchitic. Ether also produces a profound fall of blood-pressure which occurs after forty-five minutes or so of deep anæsthesia.

Chloroform is more toxic than ether, and great care is needed in its administration. I was brought up on gas-oxygen—C.E. by Boyle and it has served me well over many years. *Gas-oxygen* alone does not give abdominal relaxation, unless severe anoxia is caused. (This was entitled secondary saturation by McKesson.) Where ether is used with gas-oxygen to give relaxation, the gas-oxygen is really only a vehicle for the ether.

Trilene is not adequate for abdominal relaxation but may be used in conjunction with ether.

With *cyclopropane* relaxation is excellent, it is non-irritant and respiration is quiet. Controlled respiration is required sometimes to obtain the degree of relaxation needed for upper abdominal surgery. I must admit that I have not always been able to get the degree of relaxation required. These cases are rare, but they do occasionally occur, and then I have to add a little ether—but a little goes a long way. Nausea does follow its use and I would put it somewhere between gas-oxygen and ether in that respect. More bleeding occurs with cyclopropane in light anæsthesia, though this is not so in deep anæsthesia.

Spinal analgesia.—In the days of stovaine I saw several deaths, which I now know were due to spinal shock—profound fall of blood-pressure and to lack of controllability of the solution. Some say that they dislike spinal analgesia because of the profound fall of blood-pressure which occurs. Nowadays, however, thanks to nupercaine, spinal analgesia is absolutely controllable as to height, and the blood-pressure can be maintained at any level by means of an intravenous adrenaline drip. Headache does occur sometimes. In over 2,000 cases at St. Mark's I found the incidence of post-operative headache to be 2·8%. Nupercaine will give some two hours' analgesia which is of great help in the prevention of pain impulses and of shock.

solution at body temperature is slightly lighter than the C.S.F., but its admixture with that fluid must rapidly render this difference insignificant. As the solution leaves the point of the needle, however, its immediate route is determined by its levity and so it starts to pass up the posterior compartment of the theca. In this movement it is aided by the displacement of fluid towards the cranium which of necessity must occur when additional fluid is injected into the cavity of the spinal theca, rigidly closed at its lower end. A further directive influence is exerted by the imperfect division of the thecal cavity by the nerve roots and the dentate ligament. In this way the fluid first passes up the posterior aspect to the highest point and then some of it, by now rather diluted, actually descends for a limited distance the dorso-cervical limb of the curve so that it reaches the highest dorsal and even the lowermost cervical nerve roots. That a light solution can actually overstep the highest point of the curve is demonstrated in every case, it is due to the displacement factor and also, in lesser degree, to the fact that, like the bubble of a spirit level, it has to be balanced on both sides of the highest point.

It is usually accepted that a spinal anæsthetic acts upon the nerve roots and not upon the cord itself. This is in the main true, it is shown by the fact that the anæsthesia is zonal in its distribution and that parts below the level have normal sensation and movements, indicating that the conducting tracts are not affected. That the nerve roots are so readily susceptible to the anæsthetic is, I believe, explained by their division into fine bundles as they enter and leave the cord, and not by any special sensitivity of the nerves in this region. It is, however, beyond dispute that the cord itself is ultimately affected since definite degeneration of the more superficial tracts can be seen in sections of the cord in animals after large doses of 10% procaine. This in itself is, to my mind, an argument in favour of the use of dilute solutions as opposed to smaller quantities of more concentrated anæsthetic, and is an obvious warning against the use of solutions artificially levitated by such materials as alcohol.

Two further points must be noted. The extent of the anæsthesia obtained by this method is from D.1 to L.3; this would appear more than sufficient to cover the whole of the somatic supply to the abdominal wall and the splanchnic supply to the viscera. There remain, however, the sensory fibres of the vagus and phrenic nerves. The latter rarely cause much trouble, although careless swabbing under the diaphragm produces the usual shoulder tip pain. No special action is necessary beyond gentleness in this region. The sensory fibres of the vagus transmit a sensation of intense nausea and faintness when stimulated either by the surgeon's manipulations or the exaggerated intestinal peristalsis due to the withdrawal of sympathetic control. This is diminished by the periœsophageal injection of some of the solution after the abdomen is opened, blocking both right and left abdominal vagi at this level.

The second point concerns the use of vasopressor substances in an attempt to limit the fall of blood pressure. Although I am not entirely convinced concerning the value of ephedrine in this respect I routinely give 1 gr. 20 minutes preoperatively. It is certainly theoretically correct. In any case I believe that active vasopressor agents, such as adrenaline, methylisothiourea or veritol should always be available when a spinal anæsthetic is being given.

From what has already been said spinal anæsthesia can be claimed as a simple method, requiring no special appliances other than those essential for any spinal puncture. Of its safety a good deal of evidence is available. I have myself used the method in over 700 cases without fatality and with little anxiety. By the kindness of other administrators and from published articles, I have been able to collect nearly 2,000 records with the same happy result. Two deaths have been brought to my attention, however, with full details of the administrations. In neither could I detect any fallacy in the technique, nor did the post-mortem examinations adequately explain the cause of death.

The final point is reliability. Unfortunately it cannot be claimed for any type of spinal anæsthesia that it is utterly reliable. Even in the most experienced hands there occurs a very small percentage of cases where, owing to ossification of ligaments the theca cannot be entered, and a still smaller number where proper penetration of the dura is followed by failure. In the above series the failures have to be reckoned in decimal points, so that it is not a very serious indictment of the method. Opportunities for determining the reason for the very rare failures are, of necessity, rarer still, but it so happens that in two cases I have been fortunate enough to be able to do so; in both there was an anatomical abnormality to account for the failure and there was no need to assume any condition of "rachi-resistance" such as Sebrechts suggested.

Paradoxically enough I have noted that the commonest cause of failure is not of the anæsthetic but of the administrator's recognition that his case is anæsthetized. A

patient under a spinal anæsthetic may refer sensations to his abdominal wall in the same way than an amputee feels his phantom limb, so that it is common experience for a patient to explain that he can still feel quite well while the surgeon makes an extensive , incision which entirely fails to attract any attention.

The final point to be mentioned is the psychological aspect. There is no denying that the performance of an extensive operation under this form of anæsthesia is somewhat of an ordeal for the patient, yet I have been very impressed by the large percentage who, when offered gas and oxygen after the operation has been started, reply that they would rather carry on without it. In the last 100 cases, for instance, supplementary general anæsthetics were used in 24, and of these a considerable number were given at the instigation of the surgeon, not because the patients wished it. The preliminary morphia of course helps, but more important is the proper psychological atmosphere in the theatre, and this must be the constant concern of the administrator.

One disadvantage of spinal anæsthesia, especially noticeable in a teaching hospital, is that talk about the operation or the case must be very guarded and scanty.

Nervous sequelæ have not been frequent in the present series. Headaches lasting more than a day or two have been rare, one VIth nerve palsy had not completely recovered at the end of six months, urinary disturbances have been trifling.

Because it avoids, or minimizes, those difficulties and sequelæ of which I spoke at the beginning, I believe that the advantages of high spinal anæsthesia outweigh by far such disadvantages as have been mentioned; I have therefore used it routinely over many years for all gastrectomy and similar operations with increasing satisfaction as time goes on.

Mr. Frankis Evans: Anæsthesia in abdominal surgery must be considered essentially in terms of relaxation. Abdominal relaxation may be obtained in many ways—by inhalation anæsthesia, intravenous anæsthesia, spinal analgesia and regional analgesia, either as a field block of the abdominal wall or as a posterior intercostal block.

Of the inhalation anæsthetics, what has the anæsthetist to choose from? Ether, chloroform, trilene and cyclopropane.

Ether has served us well in the past, but pulmonary complications have been frequent and it is an irritant. 65% to 72% of patients are said to vomit following ether. The chesty patient does not do well on ether. Ether *is* an irritant. It has been shown however, that pulmonary complications follow high spinal and regional analgesia and they even occur after cyclopropane which is non-irritant. Even admitting all that, I still feel that it is wrong to give ether to a chronic bronchitic. Ether also produces a profound fall of blood-pressure which occurs after forty-five minutes or so of deep anæsthesia.

Chloroform is more toxic than ether, and great care is needed in its administration. I was brought up on gas-oxygen—C.E. by Boyle and it has served me well over many years. *Gas-oxygen* alone does not give abdominal relaxation, unless severe anoxia is caused. (This was entitled secondary saturation by McKesson.) Where ether is used with gas-oxygen to give relaxation, the gas-oxygen is really only a vehicle for the ether.

Trilene is not adequate for abdominal relaxation but may be used in conjunction with ether.

With *cyclopropane* relaxation is excellent, it is non-irritant and respiration is quiet. Controlled respiration is required sometimes to obtain the degree of relaxation needed for upper abdominal surgery. I must admit that I have not always been able to get the degree of relaxation required. These cases are rare, but they do occasionally occur, and then I have to add a little ether—but a little goes a long way. Nausea does follow its use and I would put it somewhere between gas-oxygen and ether in that respect. More bleeding occurs with cyclopropane in light anæsthesia, though this is not so in deep anæsthesia.

Spinal analgesia.—In the days of stovaine I saw several deaths, which I now know were due to spinal shock—profound fall of blood-pressure and to lack of controllability of the solution. Some say that they dislike spinal analgesia because of the profound fall of blood-pressure which occurs. Nowadays, however, thanks to nupercaine, spinal analgesia is absolutely controllable as to height, and the blood-pressure can be maintained at any level by means of an intravenous adrenaline drip. Headache does occur sometimes. In over 2,000 cases at St. Mark's I found the incidence of post-operative headache to be 2·8%. Nupercaine will give some two hours' analgesia which is of great help in the prevention of pain impulses and of shock.

For upper abdominal analgesia I use the heavy percaine 1·8 c.c. expanded to 2 c.c. with C.S.F. injected intrathecally in the 2nd or 3rd lumbar interspace. The patient is placed in a 5 degree Trendelenburg position for five minutes. In lower abdominal surgery the full Trendelenburg position is not to be used under fifteen minutes, by which time the anæsthetic is safely fixed.

The adrenaline drip consists of 1 in 250,000 adrenaline in normal saline which is administered intravenously. It is advisable to add the adrenaline to the saline after having got the drip going, and to bubble some CO_2 through the saline before use. Hospital saline tends to cause the adrenaline to become oxidized as shown by a pink colour and failure to keep the blood-pressure raised. The acidifying of the saline by the CO_2 prevents this. Vacoliter and sterivac saline, on the other hand, do not cause this adrenaline breakdown. The average rate of drip required is some 50 or 60 per minute. The drip is continued post-operatively until the patient's own blood-pressure control mechanism returns to normal function. This latter point in technique is important.

Intravenous pentothal has revolutionized anæsthesia. Full abdominal relaxation can be obtained with it, and it is possible to perform major abdominal operations under continuous pentothal. I have used it for a partial gastrectomy. The patient was frail, and did not require more than 1 g. during the whole operation of 1 to 1¼ hours. On the other hand, I would not use it on the tough soldier because he would need too much pentothal in too short a time. I personally always use omnopon and scopolamine 1/3 gr. and 1/150 gr., 1 hour pre-operatively when pentothal is to be used (except for urinary patients when the scopolamine is omitted).

Abdominal field block in combination with gas-oxygen or pentothal I have found excellent, provided the surgeon is careful and gentle of touch. Posterior intercostal block combined with splanchnic block will be dealt with by Dr. Baker. Personally, I think that if a splanchnic block is to be used one might just as well use a spinal, as the blood-pressure fall is the same.

It will be seen from the foregoing that we have many methods of anæsthesia from which to choose, and I would like to enumerate now some of the factors that influence our choice:

(1) *The operation to be performed.*—Obviously a chronic appendix can be removed quite easily with a minimum of anæsthesia. On the other hand, a perineo-abdominal excision of the rectum or a partial gastrectomy require full relaxation. Intimately related to the operation to be performed is—

(2) *The condition of the patient.*—The build (fat or thin), habits (drink and tobacco) and condition of the pulmonary and cardiovascular systems all influence our choice.

(3) Thirdly, *the time factor is important.* The longer a patient is under anæsthesia the more likely is he to have unpleasant post-operative complications. I have already mentioned the blood-pressure fall with deep ether anæsthesia.

(4) *The likelihood of shock.*—Spinal analgesia will prevent the shock which occurs as a result of surgical trauma, by blocking pain stimuli.

(5) *Geographical considerations* tend to influence our choice also. We cannot expect to find all those refinements in remote districts which are to be found in the cities and towns. It may well be that the anæsthetist in that remote district may be quite *au fait* with ether, but not have had much practice with cyclopropane and field blocks, &c. This will not matter very much if the patient is reasonably fit, but if he be frail and a poor risk he should be given every chance of obtaining the best, for it may mean life or death. I am one of those people who do not like patients conscious while they are having a major abdominal operation. I should not like it myself and, therefore, I do not inflict it on others. Therefore, whatever method is chosen, unconsciousness is a *sine qua non.* In fairness to Dr. Baker, I must admit that when I saw Dr. James at work giving omnopon intravenously, the patient remarked "Doctor I have been wanting to feel like this for years", and showed no signs of mental stress while the operation was in progress.

In the choice of anæsthetic then we have to consider the induction, maintenance and provision of relaxation. I prefer intravenous pentothal for the induction of unconsciousness as a general rule. One of the contra-indications to pentothal (and there are few) is said to be severe liver damage. Personally I have used it in three cases of cirrhosis of the liver, and I found these patients burnt it away more quickly than the normal patient. I keep the patient asleep with gas-oxygen, if a spinal or intercostal or field block is to be used. On the other hand, there are those who prefer a combination of pentothal induction and a mixture of cyclopropane and continuous pentothal for maintenance of relaxation. My own preference for lower abdominal surgery such as perineo-abdominal

excision of the rectum, is pentothal induction, heavy percaine spinal for relaxation, and gas-oxygen to maintain unconsciousness. For upper abdominal surgery such as cholecystectomy or partial gastrectomy I prefer pentothal induction followed by cyclopropane. I use a high spinal on occasions, and I use intercostal block, but my impression is that patients seem fitter the next day after cyclopropane. If I myself were about to undergo any of the above-mentioned operations, the technique I have outlined is what I would prefer.

In acute intestinal obstruction the choice of anæsthesia depends upon whether the patient is vomiting severely and whether he is in good or poor shape. If the patient be vomiting, a Ryle's tube passed before operation is essential, for then the stomach can be emptied and the risk of the patient drowning in his own fluids is removed. If the patient is in good shape a medium spinal with preliminary pentothal may be used. Even so, instead of the spinal, an abdominal field block may be given together with intravenous continuous pentothal. I do not recommend pentothal for the desperate venture. The patient who has become obstructed following an abdominal operation is more easy to relax than the average healthy adult. He lacks the vital force or energy of the latter. Consequently, an abdominal field block combined with a minimal quantity of continuous intravenous pentothal carefully given will prove adequate.

Lastly, a word about post-operative pulmonary complications—bronchitis, pneumonia, and atelectasis. Pulmonary sequelæ occur whatever type of anæsthetic is used, and I do not believe they are wholly due to the anæsthetic. They are more frequent in upper abdominal surgery than in lower abdominal surgery, and occur more frequently in the winter months than in the summer. Attention to oral sepsis, post-operative inhalation of CO_2 and O_2, breathing exercises and an expectorant cough mixture will go far to minimize these distressing complications.

A sense of proportion is vital. You do not need a spinal analgesic plus pentothal and gas-oxygen to remove an appendix. Though I still use ether, I use it very much less than I did. Students, too, have to be taught!

Our aim is to put the patient to sleep comfortably, to give adequate relaxation with as little disturbance of the physiological processes as possible, and to minimize unpleasant post-operative sequelæ and complications.

Dr. A. H. L. Baker: This paper presents an interim report of upper and mid-abdominal regional analgesia induced by means of posterior intercostal and splanchnic blocks. The technique and method used follow that described by Dr. Norman R. James in his book "Regional Analgesia for Intra-abdominal Surgery". The work has been done during the past eighteen months at the West Middlesex County Hospital.

Acknowledgment is made to Dr. James for his help and encouragement. Though the technique seemed at first laborious by comparison with the speed of induction in general anæsthesia, experience has proved its value.

Technique.—The injections are made at points four fingerbreadths from the mid-line of the back. Kappis' method is used for the splanchnic block. Paravertebral lumbar blocks may sometimes be needed as well. A subcutaneous wheal is raised in the proposed line of incision.

Drug.—Amethocaine hydrochloride (syn. anethaine, decicain, pontocaine) gives analgesia and relaxation up to three hours. Compared with procaine it is 4·5 times more toxic and in dilutions × 10 equally effective and longer lasting. 300-400 c.c. are usually prepared and 0·5 c.c. (1 ampoule) 1 : 1,000 adrenaline is added.

Strength of solution.—The technique relies on a dilute solution being injected near the nerve in sufficient quantity to reach its goal by diffusion rather than the accurate placing of a small amount of a strong solution. Painful paræsthesiæ are thus avoided and toxic absorption minimized.

Dr. James recommends 1:1,000 for intercostal and 1:2,000 for splanchnic blocks, but poor risks and elderly subjects may find this too toxic and require weaker solutions. For these, solutions as weak as 1:3,000 for intercostal and 1:6,000 for splanchnic block have been found effective but only up to one and a half hours.

Emphasis is laid on the shorter action of weaker solutions. Procaine was tried but did not give long enough analgesia in most cases.

The review covers 219 cases classified as follows:—

For partial gastrectomy, both ulcer and carcinoma	104
For cholecystectomy and operations on the biliary tract	37
For gastro-enterostomy	12
For intestinal obstruction, chronic and acute	23
For perforated peptic ulcer	14
For operations on the kidney by extraperitoneal approach	6
For laparotomy	13
For miscellaneous causes	10

Advantages.—Muscular relaxation is perfect. Intra-abdominal pressure is negative. Intestines contract and fall back into the abdomen. Diaphragmatic movement is quiet and even. Bleeding is minimal.

These are most appreciated in high abdominal surgery such as partial gastrectomy. In acute intestinal obstruction and suture of perforated peptic ulcer, the operations are more easily and speedily performed than with even a good general anæsthetic; postoperative complications, pulmonary in particular, are much less. The more dilute solutions have been found adequate, and even preferable, in such cases. Patients with perforated peptic ulcer appreciate the earlier relief of abdominal pain if the splanchnic injection is made first. The intercostal blocks are then better tolerated.

Supplementary general anæsthesia.—Light anæsthesia is not always entirely controllable over long periods and restlessness, coughing and retching have been experienced to the surgeon's discomfort. Deeper anæsthesia may then be necessary, largely neutralizing the advantages of the regional.

Sedation by injections of omnopon (pantopon) gr. 1/3 is preferable. Pre-operatively this is given hypodermically one hour before operation and repeated three-quarters of an hour later in robust patients. Further doses by the intravenous route may be given during operation but care must be taken to avoid overdosage. A total of omnopon gr. ii has been well tolerated in a few cases. Hyoscine gr. 1/150 given pre-operatively tends to cause restlessness and has been given up.

During a long operation, it is important to support the lumbar region with a small pillow and to keep the limbs comfortable. The mouth should be kept moist and tepid sponging of face, neck and arms is comforting in a hot operating theatre.

Oxygen, given continuously by B.L.B. mask or other suitable apparatus, helps to maintain a good general condition.

The blood-pressure is sometimes found to fall, due to the splanchnic block. If it drops below 80 mm.Hg systolic, intravenous injections of ephedrine (gr. ½-1) may be used to raise it again; maintenance at approximately 100 mm. systolic and 70 mm. diastolic is satisfactory. This all may be largely prevented by giving intramuscular ephedrine before the block.

Traction on the œsophagus often causes transient nausea.

After operation, the patient is placed semi-recumbent in bed for two hours and then in Fowler's position. A small cup of sweetened weak tea is often acceptable and of good psychological value if surgically permissible. Oxygen therapy is maintained for at least forty-eight hours, combined with regular breathing exercises and coughing up of secretions under supervision of the ward staff; this minimizes risk of chest complications.

Although some patients dislike the idea of remaining conscious during operations, the majority, if well looked after, tolerate regional analgesia well, and are pleased with the results and at being spared recovery from general anæsthesia. The ability of the patients to control their own airways at once on return to the ward is a great advantage in the present shortage of nursing staff.

Local Anæsthesia

Mr. Harold Dodd demonstrated three essentials of a technique of local anæsthesia which he had used since 1937 with consistent satisfaction.

The apparatus consists of a baby's feeding bottle which is available in all hospitals and is used because it is made of glass which stands autoclaving.

Pressure tubing, connecting the bottle to—

5-c.c. *syringe* with a two-way valve. The 5-c.c. syringe is used because of the ease with which injections are made and it permits a delicacy of touch from which it is possible

to estimate the tissues which are penetrated. The needle is the ordinary No. 15 to 17 hypodermic.

Anæsthetic materials used—

Novocain ½ to 1%	Acts: Immediately Duration: 40-60 minutes Toxicity: Nil
Amethocaine 1:1,000	Acts: In 5 minutes Duration: 1½-2½ hours Toxicity: Slight
Nupercaine 1:1,500-2,000	Acts: 10-15 minutes . Duration: 2-4 hours Toxicity: Fair in this dilution
Adrenaline 1:1,000 ...·· ·	One or two minims per oz. added after sterilizing, as it is destroyed by boiling; ½ minim per oz. for opera- tions on the neck

Sterilization.—All by boiling or autoclave.

Gross amounts usable.—All 200 c.c. with safety and same volume again, after 10 minutes.

The injection.—The injection is a combination of regional field block plus direct infiltration into the area of the operation. The regional field block is made again with the hypodermic needles, 6-7 c.c. per puncture. The needle is entered in the mid-axillary line opposite the umbilicus and is gradually thrust in hard. up to its shoulder. This infiltrates the XIth nerve. There is no danger of perforating peritoneum because here this membrane is singularly mobile and is readily lifted by the stream of anæsthetic. The needle is then all but withdrawn and reinserted, pointing along to the undersurface of the costal margin, again thrusting the needle hard to its shoulder. This infiltrates the Xth nerve. Again the needle is all but withdrawn and reinserted this time hard in the direction of the pubic spine. This blocks the XIIth nerve. For both upper and lower injections care is taken to advance the needle slowly to avoid it snapping off by the shoulder by forcible contact at the costal margin or the iliac crest. Direct local infiltration is made in the line of the incision. 3 c.c. are placed under the skin raising the pig-skin wheal and 3 c.c. vertically down passing through the full thickness of the abdominal wall.

When the abdomen is opened, the liver is retracted by a Pannett's elevator and with a lumbar puncture needle on the syringe an injection of 40 to 50 c.c. is made at the upper border of the pancreas in the middle line, the index finger of the left hand pressing the aorta to the left and the inferior vena cava to the right. Suction is exercised on the syringe before making the injection, to be sure the needle has not entered a large vessel.

A supplementary anæsthetic is necessary for the exploration of the abdomen and the open ether sleep has been found best for this. It is safer than pentothal and superior to gas and oxygen. Closed anæsthesia has the effect of tightening up the abdominal musculature. It has not been possible to explore the abdomen adequately and painlessly by the local anæsthesia alone. Open ether sleep means that no gag, air-way or tongue forceps are used. It is discontinued after the exploration. The method has robbed upper abdominal operations of all problems of tension in the abdominal musculature and between surgeon and anæsthetist.

Mr. W. Etherington-Wilson: Since I introduced my technique here in 1934, an extended experience of controlled block in 1,600 cases still suggests that spinal analgesia deserves more notice, more study, more sorting out of methods and a realization everywhere that slap-dash qualification has no place in this subject. American medical officers have remarked that spinal block must be unpopular in England as they had been unable to see it in use. This combined meeting is *the* right place to stress the absolute necessity of the very greatest sympathy, appreciation, knowledge and co-operation of surgeon and anæsthetist: an excellent example of a situation requiring team work, for the application extends to all present in the operating theatre.

The technique used must be controllable. The only possible definition of such control is a method which is adaptable in the simplest way, for hitting off *any* required nerve segment level, approximately or accurately. Intelligent care for all the finer. details

of the art and an insistence on the full complement of apparatus to hand, are necessary supplements.

Simple though any technique which has proved its worth may appear, it is still vital that absolute attention to detail must be given. Hurried modifications are all too common, often undesirable and some criticisms utterly stupid. Since the introduction of the timed vertical ascent of a hypobaric solution ten years ago at the Royal Society of Medicine and, shortly after, in Canada and the U.S.A., greater experience has not led to any fundamental changes. It would be out of place here to detail such advances or alterations. I use spinocaine in addition to the two solutions of nupercaine (1:1,500 and 1:2,000) which I use in adults. In a small series of abdominal cases in babies I have used nupercaine 1:2,500, a solution prepared in 1935, and I have come to the conclusion that spinal analgesia has a useful place in young subjects.

Many years ago, the measurements of the back lengths led to the discarding of guess-work with regard to dosage and timing in *all* cases. The simple formula below has proved its worth. Only one measurement is required, that of the high spinal run, from the space used (lumbar 3 or 4) to the 4th thoracic spine. Anatomically, a low spinal block is approximately half this distance (12 T. 1 L. segments). A medium block is three-quarters of this length (9-10 thoracic segments). Intermediate levels are often required between these better known levels. The 7th cervical vertebra in an adult of average height is four inches distant from the 4th thoracic spine and for ease of measurement in some cases, especially the adipose, the prominent spine is used entirely and four inches deducted. Any idea of smaller doses for women is ridiculous; many women have longer backs than men and a child of 13 years may have an adult back measurement. From experience and tests, nupercaine solutions (s.g. 1·003) travels to the high level at an overall rate of 5 seconds to the inch (using 13-14 c.c. nupercaine). 2 c.c. spinocaine (s.g. less than 1) travels the same distance at an average rate of 2 seconds to the inch. Such dosage, for simplicity, is used for all cases—high, mid or low. Modifications of these doses and timing are only suggested to those well experienced in the technique. Timing commences at the same moment the solution is being introduced. The nupercaine syringe must be emptied within 15 seconds. Suppose the back measurements to be 15 inches:—

Adult dosage:

4th thoracic sp. to 4th lumbar sp. = 15 in. (19 in. to 7th C. sp.).

High spinal	=	15 × 5 = 75 seconds	Using 13-14 c.c.
Medium spinal	=	¾ of 75 = 56 seconds	nupercaine
Low spinal	=	½ of 75 = 37 seconds	(s.g. 1·003)

For spinocaine (2 c.c.) use multiple 2 = 30, 22 and 15 seconds for each level.

Section of Neurology

President—Brigadier HUGH CAIRNS

[*April 6, 1944*].

Prognosis of Peripheral Nerve Injuries

By J. St.C. ELKINGTON, M.D.

INTRODUCTION

My remarks are based upon impressions gained during the last four years in examining patients in a Centre for peripheral nerve injuries set up by the Ministry of Health. These cases now number well over 1,000. I examine all of them soon after admission and, in many cases, at intervals during their stay in hospital. After discharge the patients return for review every three months for the first year, twice during the second year, and again at the end of the third year. This method gives good opportunity for following the progress of cases and, on the whole, the follow-up arrangements made through the Ministry of Pensions and the Services have proved very satisfactory.

In dealing with a subject in which there are so many independent variables, figures are apt to give an unjustified appearance of precision and finality and to prove a less valuable guide to prognosis than the impression left by the examination of a large number of cases.

The cases admitted to the Centre include lesions of widely differing severity and causation, from simple contusion at one extreme to complete anatomical severance at the other. Between such extremes a great difference in prognosis is naturally to be expected and I shall confine my remarks to an examination of the results in those cases where the nerve has been completely divided in the initial injury. or in which the damage was sufficiently severe to require a complete division and suture at the time of operation: that is to say to the results of secondary nerve suture. As regards the prognosis in incomplete lesions, whether due to contusion of the nerve or to penetration of its structure without complete division, I have on the whole been impressed by the remarkable extent to which such a nerve may recover of its own accord; the spontaneous recovery of an injured nerve is often as surprising and gratifying as that of a sutured nerve is disappointing. Further, it is proper to distinguish clearly between recovery of function in an injured peripheral nerve, and the recovery of function in the part innervated by it, and these two aspects of the problem will be considered separately.

FACTORS INFLUENCING RECOVERY IN A DIVIDED PERIPHERAL NERVE

Anyone who has examined a large number of peripheral nerve injuries over a period of time cannot but have been impressed by the very great variety in the ultimate result and it will serve as a useful point of departure to describe what may be considered to be the normal expectation of recovery in the individual nerves most commonly injured, when they have been sutured under favourable conditions. We can then consider additional factors which may influence the average result either favourably or unfavourably.

Radial nerve.—The radial nerve is by common consent in a class apart and the results of suture of this nerve are incomparably better than those of any other. In an uncomplicated suture of the radial nerve trunk in the arm one can safely predict a satisfactory

AUG.—NEUR. 1

recovery of function in all the muscles innervated by it, including the three long extensors of the thumb. It is true that the muscles do not, in the majority of cases, recover their full former strength so that there may be a considerable residual disability in the case of heavy manual workers; but for those who are not called upon to exercise great muscular strength, the results are extremely satisfactory. It is an unfortunate fact that the anatomical arrangements of the radial nerve in its distal part make suture at that level difficult, and for this reason the prognosis of injuries to its important dorsal interosseus branch are poor compared with those of the main trunk. However, the results of radial nerve suture are such that every effort should always be made to secure end-to-end reunion of this nerve before other procedures, such as tendon transplants, are embarked upon, however satisfactory these may be in themselves.

Ulnar nerve.—At the other end of the scale in the upper limb is the ulnar nerve, where the results of suture are on the whole extremely disappointing. This is the more surprising as the nerve pursues a superficial course, is readily accessible and is often severed in injuries which cause minimal damage to surrounding tissue and little loss of continuity in the nerve. Following suture of the nerve in the arm it is usual to see good recovery of movement in the flexor carpi ulnaris and the portion of the flexor profundus destined for the little finger, together with recovery of sensibility to pin-prick and extremes of temperature in the ulnar cutaneous area, and occasionally recovery of sensibility to touch. But very rarely indeed does one see any effective recovery of voluntary movement in the ulnar intrinsic muscles of the hand. This is equally true of lesions of the ulnar nerve in the forearm or at the wrist; and as the innervation of the intrinsic muscles represents the principal contribution of the ulnar nerve to function, the permanent disability is considerable.

Median nerve.—Intermediate between the radial and ulnar nerves is the median. This is less frequently divided without associated tissue damage than is the ulnar, and yet the functional results of suture are more satisfactory. In lesions in the arm it is usual to see a good recovery in pronator teres, flexor sublimis and profundus and even flexor longus pollicis. The median intrinsic muscles of the thumb, like the ulnar intrinsics, seldom make a satisfactory recovery, but in their case the functional disability is slight. On the sensory side, recovery of crude sensation to pain and temperature is the rule and in a considerable number of cases there is some recovery of sensibility to light touch. In a small minority this proceeds to a point where the lightest stimulus is appreciated and in these compass-point discrimination at 1 cm. or even ½ cm. may become accurate in the affected finger tips. The principal contribution of the median nerve being its innervation of the forearm muscles and in the provision of a considerable portion of the sensation of the hand, the practical result is thus fairly satisfactory.

Sciatic trunk.—In the lower limb the three principal lesions encountered are those of the sciatic trunk in the thigh and of its terminal branches, either in the popliteal space or in the leg. Lesions of the sciatic trunk often lend themselves to satisfactory suture, but the results seldom justify the surgeon's hopes or the patient's expectations. It is usual to see reasonable recovery of voluntary power in the gastrocnemius and soleus and often some in tibialis posterior. These muscles together provide fair plantar flexion at the ankle although with an abnormal inversion of the foot. Recovery in the flexors of the toes is very exceptional and I do not remember having ever seen any in the intrinsic muscles of the foot. The muscles innervated by the peroneal nerve are even more disappointing. In the majority of cases no recovery at all occurs; but in some weak contraction appears in tibialis anterior and the peronei and even occasionally in the dorsiflexors of the toes. The combined action of these muscles, however, is seldom sufficient to dorsiflex the foot against the action of gravity and so does not enable the patient to dispense with a toe-elevating device. On the sensory side there is commonly recovery of crude sensation to pin-prick and temperature in the distribution of the sciatic nerve including the sole, which serves to protect the foot to some extent from blisters and other injuries, but often at the price of a good deal of spontaneous discomfort and of aching after exertion. The foot remains an inefficient instrument. The arches become depressed and callosities develop under the metatarsal heads and readily give rise to infected corns and ulcers.

Peroneal nerve.—Lesions of the terminal branches of the sciatic give results in their respective areas very comparable with those of the sciatic trunk. The poor results of peroneal suture are the more disappointing owing to the superficial position of the nerve and the frequency with which it is divided with little surrounding damage. A fair sensory recovery is the rule, but in many cases the muscles of the anterior and lateral tibial compartments remain totally inactive, and in the majority so weak as not to give any useful recovery of function.

Tibial nerve.—In the case of the tibial nerve the return of crude sensibility in the sole can be expected, but muscular recovery seldom proceeds beyond the proximal muscles of the calf.

Generalizations.—From these observations it is permissible to make two generalizations:—

(1) That the smaller the muscle and the more delicate its function the less likely it is to make a satisfactory functional recovery after a period of denervation. This is in conformity with the relative recovery of function seen after lesions or injuries to the central nervous system. It might be suggested that the important factor is merely the distance which the new fibres have to grow, since the small muscles with delicate functions are, in fact, those situated in the periphery of the limb. Against this interpretation, however, is the fact that the prognosis seems to be no better when the nerve is divided distally, as for example in lesions of the ulnar nerve at the wrist; and again the distance does not seem to interfere with the restoration of sensory function in the distal area. anything approaching complete restoration, nevertheless it represents an improvement progress seems to be little influenced by the distance they have to travel.

(2) That on the whole, from a functional point of view, sensory recovery is more reliable and more satisfactory than motor recovery and although it seldom proceeds to anything approaching complete restoration, nevertheless it represents an improvement which in most cases, in itself, justifies the suture of a mixed nerve.

Consideration of Factors Modifying the Average Prognosis in Common Peripheral Nerve Injuries

(1) *Nature of Wound.*—Unfortunately many peripheral nerve injuries are not clean surgical divisions but are complicated by heavily infected compound fractures, by severe destruction of the soft tissues, or by considerable loss in continuity of the nerve itself. All these factors affect very adversely the prognosis in nerve suture. The presence of a large amount of scar tissue or the loss of the normal muscular bed in which the nerve lies, greatly decreases the prospect of recovery. Even more so does loss of continuity in the nerve itself, necessitating complicated manœuvres and extensive dissections to enable the ends to be approximated. One has seen many ingenious surgical procedures adopted to overcome this gap, but my impression is that the more they are necessary, the less are they worth while.

(2) *Date of suture.*—The period of time elapsing between division and secondary suture of a nerve is a factor which might be expected to have an important influence on the final outcome. It has been our practice to allow the minimum of three months to elapse between complete healing of the wound and an attempt at suture. This rule has been observed to avoid any possibility of operating on infected tissue. In many cases the interval has, in fact, been longer for patients may have travelled for many months before arriving at the Centre, and since they are often admitted in fairly large groups a surgical bottleneck is apt to be created which has tended to prolong the period before suture. On only one occasion has sepsis been encountered which suggests that on the whole we have been more conservative than is necessary on this account. If it could be shown that cases do better with earlier suture the fear of sepsis should not delay operation in the future as long as it has done in the past. On this point I have little information, but in the earlier years of the war when cases were fewer and surgeons' knives were sharper, some cases were operated on considerably earlier. Again, cases turn up from time to time which have been sutured elsewhere within a shorter time of their injury, and I have the impression that the results have been more favourable than the average.

(3) *Individual factors.*—It is reasonable to suppose that in nerve regeneration as with any other process of healing, individuals may vary: but of the factors responsible for this variation only one will be mentioned, namely the age of the patient. Our cases have included a number of air-raid and other injuries in children under the age of 15 and a good many Service cases under the age of 20. They have left the strong impression that, other things being equal, the younger the patient, the better the outlook. Vice versa the prospects of recovery in elderly people are extremely poor, and one doubts whether suture of peripheral nerves is of real value after the age of 50.

In examining our results it is very striking how often in the cases which do better than the average one finds one or both of these factors—a youthful patient or an early suture.

(4) *The surgeon.*—A factor in prognosis which a physician can only mention with some diffidence is the surgeon performing the operation. Naturally, working at one centre, one has had the greatest opportunity of observing the results of one surgical team,

recovery of function in all the muscles innervated by it, including the three long extensors of the thumb. It is true that the muscles do not, in the majority of cases, recover their full former strength so that there may be a considerable residual disability in the case of heavy manual workers; but for those who are not called upon to exercise great muscular strength, the results are extremely satisfactory. It is an unfortunate fact that the anatomical arrangements of the radial nerve in its distal part make suture at that level difficult, and for this reason the prognosis of injuries to its important dorsal interosseus branch are poor compared with those of the main trunk. However, the results of radial nerve suture are such that every effort should always be made to secure end-to-end reunion of this nerve before other procedures, such as tendon transplants, are embarked upon, however satisfactory these may be in themselves.

Ulnar nerve.—At the other end of the scale in the upper limb is the ulnar nerve, where the results of suture are on the whole extremely disappointing. This is the more surprising as the nerve pursues a superficial course, is readily accessible and is often severed in injuries which cause minimal damage to surrounding tissue and little loss of continuity in the nerve. Following suture of the nerve in the arm it is usual to see good recovery of movement in the flexor carpi ulnaris and the portion of the flexor profundus destined for the little finger, together with recovery of sensibility to pin-prick and extremes of temperature in the ulnar cutaneous area, and occasionally recovery of sensibility to touch. But very rarely indeed does one see any effective recovery of voluntary movement in the ulnar intrinsic muscles of the hand. This is equally true of lesions of the ulnar nerve in the forearm or at the wrist; and as the innervation of the intrinsic muscles represents the principal contribution of the ulnar nerve to function, the permanent disability is considerable.

Median nerve.—Intermediate between the radial and ulnar nerves is the median. This is less frequently divided without associated tissue damage than is the ulnar, and yet the functional results of suture are more satisfactory. In lesions in the arm it is usual to see a good recovery in pronator teres, flexor sublimis and profundus and even flexor longus pollicis. The median intrinsic muscles of the thumb, like the ulnar intrinsics, seldom make a satisfactory recovery, but in their case the functional disability is slight. On the sensory side, recovery of crude sensation to pain and temperature is the rule and in a considerable number of cases there is some recovery of sensibility to light touch. In a small minority this proceeds to a point where the lightest stimulus is appreciated and in these compass-point discrimination at 1 cm. or even ½ cm. may become accurate in the affected finger tips. The principal contribution of the median nerve being its innervation of the forearm muscles and in the provision of a considerable portion of the sensation of the hand, the practical result is thus fairly satisfactory.

Sciatic trunk.—In the lower limb the three principal lesions encountered are those of the sciatic trunk in the thigh and of its terminal branches, either in the popliteal space or in the leg. Lesions of the sciatic trunk often lend themselves to satisfactory suture, but the results seldom justify the surgeon's hopes or the patient's expectations. It is usual to see reasonable recovery of voluntary power in the gastrocnemius and soleus and often some in tibialis posterior. These muscles together provide fair plantar flexion at the ankle although with an abnormal inversion of the foot. Recovery in the flexors of the toes is very exceptional and I do not remember having ever seen any in the intrinsic muscles of the foot. The muscles innervated by the peroneal nerve are even more disappointing. In the majority of cases no recovery at all occurs; but in some weak contraction appears in tibialis anterior and the peronei and even occasionally in the dorsiflexors of the toes. The combined action of these muscles, however, is seldom sufficient to dorsiflex the foot against the action of gravity and so does not enable the patient to dispense with a toe-elevating device. On the sensory side there is commonly recovery of crude sensation to pin-prick and temperature in the distribution of the sciatic nerve including the sole, which serves to protect the foot to some extent from blisters and other injuries, but often at the price of a good deal of spontaneous discomfort and of aching after exertion. The foot remains an inefficient instrument. The arches become depressed and callosities develop under the metatarsal heads and readily give rise to infected corns and ulcers.

Peroneal nerve.—Lesions of the terminal branches of the sciatic give results in their respective areas very comparable with those of the sciatic trunk. The poor results of peroneal suture are the more disappointing owing to the superficial position of the nerve and the frequency with which it is divided with little surrounding damage. A fair sensory recovery is the rule, but in many cases the muscles of the anterior and lateral tibial compartments remain totally inactive, and in r· majority so weak as not to give any useful recovery of function.

suture or simple neurolysis was carried out. All cases of officers and Naval and R.A.F. personnel have been excluded so that the results apply solely to the N.C.O.s and men in the Army.

There were altogether 143 such cases. Of these 125 were invalided out of the Army from hospital. 18, of whom 14 were ulnars, were returned to duty in a lower category and of these a further 3 were placed in Cat. E during the ensuing year. It thus appears that a soldier or N.C.O. having a peripheral nerve injury sufficiently serious to require exploration has just over a 10% chance of being of further service to the Army in a lower category. This is a point which may be of some value in reaching an early decision as to disposal.

SUMMARY

It may seem that I have painted a rather sombre picture, particularly when we remember the opening words of the report of the Medical Research Council of 1920 on the subject of peripheral nerve injuries:—

> "Most cases of injury to the peripheral nervous system make a good recovery, provided that treatment is carried out systematically and over a long period of time"

but I suggest we have been inclined to expect too much. We are apt to regard a peripheral nerve as a simple structure, perhaps from comparing it unconsciously with the central nervous system in all its complexity; but, in fact, a peripheral nerve is by no means a simple structure and if the results of nerve suture were compared with those of suture of the divided ureter or bile-duct or perhaps to the attempts at repair of an injured joint, the results might appear less unfavourable. One must accept the fact that there are degrees of injury to specialized tissue which nature is incapable of repairing, and our wonderment should lie not in the fact that so many cases do so badly but that any do so well.

The Effect of Delay on the Success of Nerve Suture

By J. Z. YOUNG, M.A.

(Dept. of Zoology and Comparative Anatomy, Oxford)

THERE is abundant evidence that some degree of recovery can take place after a nerve has been sutured at long periods after injury. Perhaps because of this fact there has been a feeling that there is no great harm in waiting before operating on an injured nerve. The majority of cases, in this war as in the last, have been operated after considerable delay, probably usually after more than six months. There are possible advantages to be obtained by waiting to repair a nerve in the hope of spontaneous recovery and to allow other tissues to heal, but we shall only be justified in delaying if it can be shown that the degree of recovery is equally satisfactory whatever the time of denervation. If we examine the various stages of recovery, however, we find reason to suppose that several of the processes which produce a full functional regeneration become much less active during the atrophy of denervation.

The actual power of outgrowth of nerve fibres from the central stump, the *vis a tergo* of Held remains little diminished even in a stump left unsutured more than a year (Holmes and Young, 1942). According to our present ideas the putting out of new fibres is essentially a process of flowing of axoplasm from the tubes of the central stump, and there is no special reason to think that this power of flow would diminish with time.

The union between the apposed nerve stumps is made chiefly by the activity of the cells of Schwann, growing out from the peripheral stump. Abercrombie and Johnson (1942) have measured this power of wandering in stumps left to atrophy for various periods. They confirm Ingebrigsten (1916) in finding that Schwann cells do not migrate out from a piece of normal nerve explanted in vitro, but that in a severed nerve the power of movement increases rapidly from about the fourth day, reaching a maximum after the end of the third week and thereafter declining, at first rapidly, later more slowly. From these facts it is reasonable to expect that nerve suture may be most successful when performed some two or three weeks after injury. Holmes and Young (1942) found

but the junior personnel has varied considerably from time to time. Further, the system of follow-up on a regional basis has allowed one to observe comparable results from other peripheral nerve centres, and, since the repatriation of prisoners of war, quite a number of cases have been seen whose nerves were sutured by our own R.A.M.C. officers, or by Belgian, French or German surgeons. So far no significant difference has been detected. From the physician's point of view this is satisfactory for it enables him to remain aloof from the discussion as to whether peripheral nerve injuries are properly the province of the orthopædic surgeon, the neuro-surgeon or the general surgeon! The important point is that anyone chosen to do this work should be richly endowed with patience, and should have a lively interest in the case as a whole as well as in his nerve injury. This is a point which might well be borne in mind should it ever again be necessary to provide for the treatment of a large number of cases of this kind.

Prognosis as regards the Function of the Part Innervated

The distinction between the recovery of function in a nerve and the recovery of function in the part innervated by it is important and we do well to remember that a peripheral nerve is a means to an end and not an end in itself. The function of the parts innervated by a peripheral nerve is essentially dependent upon mobility, and if mobility is lost beyond restoration no amount of recovery in a peripheral nerve will be of service to the patient, however gratifying it may be to his doctor. The prime object in the treatment of peripheral nerve injuries is therefore the preservation throughout of the most complete possible degree of mobility of every part of the limb affected, and mobility is more easily preserved than it is recovered if once it is lost. Of the factors predisposing towards *immobility* perhaps the most common and important is splintage. It is obvious that in many limb injuries splintage is indispensable in the treatment of the associated injuries but the fewer splints that are used the better as far as the peripheral nerve injury is concerned. A case can be made out for the use of a short cock-up splint at the wrist in radial palsies, or a dorsiflexion splint for the ankle in sciatic and peroneal palsies and for shoulder abduction splints in paralyses of the deltoid; but even these should not be worn continuously. No splint should interfere with the full range of passive movements of the fingers and toes, which should be moved both actively and passively as much as possible from the outset. Where combined injuries of the bones and peripheral nerves necessitate splintage, the immobility should be reduced to the minimum that is essential for the treatment of the bony condition. The other factor making for immobility is undoubtedly pain, and it is particularly in severe lacerated wounds of the forearm and the leg, where movement of the digits causes stretching of injured muscles that the most severe contractures take place. As regards the factors which preserve mobility: Active and passive movements carried out from the earliest possible time and continued throughout the period of denervation are unquestionably the most important; such additional treatment as massage, heat and electrical stimulation are only auxiliary to this, though they may be of great value in restoring movement which has been lost. One has often been impressed in examining repatriated prisoners of war by the extraordinary mobility of their extremities, even several years after the injury. I have asked them what treatment they have received and the answer has usually been "none"! To the further question: "What have you done for your hand (or leg)?" the answer has often been: "The M.O. told me to keep moving it—so I did." One may suspect that they were able to give a greater amount of time to their condition than do those of their fellows who are subjected to the full rigours of occupational therapy! It is a matter for regret how often these simple instructions to the patient himself are omitted when they are under continuous hospital care.

Psychological factors.—In the restoration of function of the part, as opposed to the recovery of the peripheral nerve, the patient's character and mental make-up play an important part. The recovery of peripheral nerve injuries is a long and tedious business and calls for much patience and endeavour on the part of the patient. Those who are intelligent and enthusiastic and anxious to make a full recovery can contribute greatly to their own improvement. In the presence of apathy, laziness or the desire to make the most of a disability for ulterior motives, no attempt to preserve function of a limb will prove successful and it is in this connexion perhaps that occupational therapy has its greatest value.

Prognosis as regards Further Army Service

To get information on this subject an analysis has been made of those of our cases in which exploratory operation was considered necessary irrespective of whether nerve

Personal Experience of Exploration and Re-exploration of Injured Nerves

By Professor J. R. LEARMONTH, F.R.C.S.Ed.

WE have a smaller experience at Gogarburn than at most of the other Centres, and it did not appear that a detailed statistical analysis of our cases would be useful.

EXPLORATION

The majority of cases have been seen after an interval sufficient to allow for evidence of regeneration. Even when this is present, there seem to us to be certain indications for exploring the injured nerve, irrespective of the clinical findings, the object being to ascertain its exact condition and to ensure as good a permanent bed for it as possible. These indications include: (1) *Previous long-continued sepsis in the wound*: All patients are given a loading dose of sulphathiazole the night before operation, and holding doses for two days. Scar tissue is excised widely and if necessary tissue planes opened up to secure if possible an intermuscular bed for the nerve. We have had only one severe post-operative infection, and that not following a war wound. (2) *When a nerve lies at the bottom of a healed "trough" wound*: In the case of the ulnar this is not uncommon. We believe the nerve should be freed, scar tissue excised and the skin and deep tissues brought accurately over the hollow. (3) *When there is a history of unusually severe bleeding from a muscle mass*: This may mean local necrosis of muscle and a late strangling effect of scar tissue; not infrequently one sees it under pronator teres. (4) *In closed crushing types of injury*: The best example of this is the "run over" involving the thigh, in which we have more than once seen the sciatic nerve tightly gripped in a collar of fibrous tissue formed from bruised and ischæmic hamstrings. (5) *When a nerve or nerves, and the main artery to an extremity, have been injured at the same level*: They are freed, any thrombosed segment of artery resected, and the various strands replaced, so far as possible, in separate "beds." (6) *When two or more nerves of the same limb have been injured*: This is especially desirable if the wound has involved a part where the nerves are running close to each other. (7) *When persistent pain or persistent hyperidrosis is present* in the cutaneous distribution of the injured nerve.

When evidence of regeneration is absent or doubtful, the length of the interval after the wound is often enough to decide for exploration. In doubtful cases we make use of curves of muscle excitability constructed for us by Dr. Ritchie, which enable us to differentiate between denervated muscle and muscle which has intact motor axons reaching it. These curves are of value in the transition period between denervation and re-innervation, and change towards the normal appears before any clinical sign of motor recovery, although the warning interval is not the same for all nerves.

We have had an opportunity of observing the effect of gross reduction in total blood supply on the possibility of recovery of nerve function. In this case the axillary, anterior circumflex humeral, and posterior circumflex humeral arteries were wounded, and musculo-cutaneous, median, musculo-spiral and ulnar nerves divided high in the axilla. Muscle biopsies showed considerable ischæmia in the abductor digiti minimi, none in pronator teres and biceps. Four months after the injury the humerus was shortened, and the distal segments of both musculo-cutaneous and median nerves were united together to the proximal segment of the median, and the other two nerves anastomosed separately. The brachioradialis began to recover in 99 days (15 cm.), the pronator teres in 186 days (19 cm.). In such cases the longitudinal blood supply of nerves must be valuable. In the last war Sir George Makins drew attention to the important part which might be played in providing a collateral circulation by such arteries as the comes nervi ischiadici and its branches.

We have found it difficult to decide for or against excision and suture in many cases of partial division of nerves. For me the hardest cases have been those involving the nerves to the hand; and in these the general plan has been to leave well alone when the motor fibres of the ulnar nerve and the sensory fibres of the median have been intact or almost intact. In partial lesions there might be a field for funicular anastomosis; but we have been able to employ this procedure in only one case, in which it was possible to diagnose a high lesion of the median, involving the contribution from the outer head. It was possible to define and free this funiculus, resect the neuroma, and secure a good anastomosis. Exploration is only indicated if a nerve which has been recovering under conservative treatment ceases to recover, especially if the partial recovery has not included a particularly useful motor function of the nerve, for example the sensory

considerable evidence that when secondary suture was made after delay of some months the union of stumps was unsatisfactory. In this connexion we may mention an important technical point, namely that the shrinkage of the peripheral stump which occurs during a long period of denervation makes the proper apposition and suture of the stumps difficult.

Once the streams of axoplasm have crossed to the distal stump they proceed down the latter in the old tubes now filled with the protoplasm of the Schwann cells. The initial advance down the tubes does not seem to be much slowed after long periods of atrophy. However, the development of the new fibres to a functional condition depends on their subsequent increase in diameter and medullation. There is no doubt that these processes take place less rapidly after secondary than after immediate suture (Holmes and Young, 1942; Gutmann and Sanders, 1943). It may be that even though increase in fibre diameter is slow it ultimately becomes complete. However, in a rabbit examined ten months after secondary suture. we found the medullation still much less advanced than in a corresponding nerve after immediate suture. This delay in maturation is probably the result of the reduction in diameter of the Schwann tubes which occurs during atrophy, imposing a restriction on the inflow of axoplasm.

Even more serious effects of delay on the process of regeneration are found in the muscles (Gutmann and Young, 1944). When nerve fibres return to a muscle which has been denervated only for a short period they re-enter the old end-plates, producing a pattern of innervation very similar to the original one. However, during the progress of atrophy the muscle fibres shrink and the connective tissue around them increases. The ends of the Schwann tubes become blocked with collagen and new nerve fibres returning down such tubes do not enter the end-plates. They run on among the muscle fibres, often for long distances. Finally some of them make contact with a muscle fibre, producing new end-plates of atypical form. The resulting pattern of innervation is certainly far from normal, though the functional importance of the discrepancy remains to be investigated. Perhaps even more serious is that after long periods of denervation many muscle fibres never recover at all. Areas are seen in such muscles, even a year after re-innervation, in which nerve fibres are present but have failed to make contact with the muscle fibres, the latter having proceeded further with their atrophy and perhaps completely disappeared. The weight and volume of muscles remain much less a year after secondary than after primary suture and it seems doubtful if much subsequent addition of muscle tissue can take place.

It is certain, therefore, that delay in the performance of suture leads to delay and incompleteness of recovery during at least a year after the operation. It is very likely that the incompleteness of recovery is permanent and cannot be made up by subsequent restorative processes. Although rates and conditions of atrophy of nerve and muscle may be different in man from those examined in the rabbit, the general situation can hardly be essentially different. And no doubt atrophy also produces progressive and partly irreversible changes in the skin which will affect the result. Delay and the attendant atrophy therefore reduce the prospect of success after nerve suture. It would be most valuable to know quantitatively the extent to which it does so. We can say confidently that a suture made one month after injury is likely to produce a better result than one made six months after injury. But we do not know how much better. Animal experiment may throw some light on this question, but careful survey of suitably selected human cases will probably do more. There are indications which suggest that the rate of decline of the power of recovery is considerable and therefore that a policy of early suture may produce results which are a considerable improvement on those obtained hitherto. It does not follow from this, of course, that every nerve should be sutured immediately after it has been injured. Indeed there are some indications, for instance from the activity of the Schwann cells, that the optimum result is achieved by suture a few weeks after severance. If we ever obtain appropriate data allowing a quantitative assessment of the degree of recovery it should be possible to pursue a policy which will give the maximum chance of recovery to the patient.

REFERENCES

ABERCROMBIE, M., and JOHNSON, M. L. L. (1942) *J. exp. Biol.*, **19**, 266.
GUTMANN, E. and SANDERS, F. K. (1943) *J. Physiol.*, **101**, 489.
—— and YOUNG, J. Z. (1944) *J. Anat. Lond.*, **78**, 15.
HOLMES, W., and YOUNG, J. Z. (1942) *J. Anat. Lond.*, **77**, 63.
INGEBRIGTSEN, R. (1916) *J. exp. Med.*, **23**, 251.

Personal Experience of Exploration and Re-exploration of Injured Nerves

By Professor J. R. LEARMONTH, F.R.C.S.Ed.

WE have a smaller experience at Gogarburn than at most of the other Centres, and it did not appear that a detailed statistical analysis of our cases would be useful.

EXPLORATION

The majority of cases have been seen after an interval sufficient to allow for evidence of regeneration. Even when this is present, there seem to us to be certain indications for exploring the injured nerve, irrespective of the clinical findings, the object being to ascertain its exact condition and to ensure as good a permanent bed for it as possible. These indications include: (1) *Previous long-continued sepsis in the wound*: All patients are given a loading dose of sulphathiazole the night before operation, and holding doses for two days. Scar tissue is excised widely and if necessary tissue planes opened up to secure if possible an intermuscular bed for the nerve. We have had only one severe post-operative infection, and that not following a war wound. (2) *When a nerve lies at the bottom of a healed "trough" wound*: In the case of the ulnar this is not uncommon. We believe the nerve should be freed, scar tissue excised and the skin and deep tissues brought accurately over the hollow. (3) *When there is a history of unusually severe bleeding from a muscle mass*: This may mean local necrosis of muscle and a late strangling effect of scar tissue; not infrequently one sees it under pronator teres. (4) *In closed crushing types of injury*: The best example of this is the "run over" involving the thigh, in which we have more than once seen the sciatic nerve tightly gripped in a collar of fibrous tissue formed from bruised and ischæmic hamstrings. (5) *When a nerve or nerves, and the main artery to an extremity, have been injured at the same level*: They are freed, any thrombosed segment of artery resected, and the various strands replaced, so far as possible, in separate "beds." (6) *When two or more nerves of the same limb have been injured*: This is especially desirable if the wound has involved a part where the nerves are running close to each other. (7) *When persistent pain or persistent hyperidrosis is present* in the cutaneous distribution of the injured nerve.

When evidence of regeneration is absent or doubtful, the length of the interval after the wound is often enough to decide for exploration. In doubtful cases we make use of curves of muscle excitability constructed for us by Dr. Ritchie, which enable us to differentiate between denervated muscle and muscle which has intact motor axons reaching it. These curves are of value in the transition period between denervation and re-innervation, and change towards the normal appears before any clinical sign of motor recovery, although the warning interval is not the same for all nerves.

We have had an opportunity of observing the effect of gross reduction in total blood supply on the possibility of recovery of nerve function. In this case the axillary, anterior circumflex humeral, and posterior circumflex humeral arteries were wounded, and musculo-cutaneous, median, musculo-spiral and ulnar nerves divided high in the axilla. Muscle biopsies showed considerable ischæmia in the abductor digiti minimi, none in pronator teres and biceps. Four months after the injury the humerus was shortened, and the distal segments of both musculo-cutaneous and median nerves were united together to the proximal segment of the median, and the other two nerves anastomosed separately. The brachioradialis began to recover in 99 days (15 cm.), the pronator teres in 186 days (19 cm.). In such cases the longitudinal blood supply of nerves must be valuable. In the last war Sir George Makins drew attention to the important part which might be played in providing a collateral circulation by such arteries as the comes nervi ischiadici and its branches.

We have found it difficult to decide for or against excision and suture in many cases of partial division of nerves. For me the hardest cases have been those involving the nerves to the hand; and in these the general plan has been to leave well alone when the motor fibres of the ulnar nerve and the sensory fibres of the median have been intact or almost intact. In partial lesions there might be a field for funicular anastomosis; but we have been able to employ this procedure in only one case, in which it was possible to diagnose a high lesion of the median, involving the contribution from the outer head. It was possible to define and free this funiculus, resect the neuroma, and secure a good anastomosis. Exploration is ꞏꞏꞏ only indicated if a nerve which has been recovering under conservative treatment ꞏꞏꞏ to recover, especially if the partial recovery has not included a particularly useful ꞏꞏꞏ ꞏꞏꞏ function of the nerve, for example the sensory

contribution of the median. An even more urgent indication for exploration is the loss of some function wholly or partially recovered; this points to strangling of the nerve in scar tissue—what Foerster picturesquely called the "progressive circumvallation of the nerve".

When raw areas are present in the neighbourhood of the injured nerve, exploration can be hastened by skin-grafting. If the incision to be used will not transgress the graft, then a split skin graft does admirably. If, however, the graft is to be disturbed, then a whole thickness graft is best and provides a setting well worth the wait of six weeks or so. In these days of accomplished plastic surgery, extensive loss of soft tissue is no contra-indication to ultimate exploration, provided it is known, or can be ascertained, that suture is possible.

To be confronted with a divided nerve years after the original injury is not very uncommon. The chances of recovery are often slight, and the anastomosis technically difficult on account of the disparity between the proximal and distal segments. The longest interval we have encountered has been four years, in a patient whose ulnar nerve had been divided above the elbow. However, by the time he was sent back to Canada, 126 days later, voluntary power had returned in the flexor profundus digitorum. The ultimate prognosis is not good.

CONSERVATIVE TREATMENT

Against exploration and suture are gross loss of tendon and particularly of muscle tissue, when it is obvious that no useful movement can be restored. We have been conservative too when injury to a joint complicates the clinical picture in such a way that it cannot be postured to provide slack, as in the case of extensive injury at the knee-joint with subsequent ankylosis, with an associated lesion of the external popliteal nerve. We have not explored closed supraclavicular lesions of the brachial plexus.

RE-EXPLORATION

It is clear that each problem must be decided on its own merits, but there are certain guiding principles which we employ. Of these the first and most obvious is the interval which has elapsed since suture; although in some cases the exact level of suture is unknown, it is nearly always possible to determine, necessarily within somewhat wide limits, the period which must elapse before the suture can be considered unsuccessful. Another factor is the person of the original operator: we have been very reluctant to re-explore a nerve sutured by a surgeon of known experience in this work. Occasionally we have had to deal with nerves sutured under unsuitable circumstances, for example in the field, and then we have been less inclined to wait; and we have been guided by Professor Seddon's view, that immediate primary suture is on the whole less likely to be highly successful than suture undertaken after a short interval.

When recovery seems to be delayed, it is natural to go back over the steps of the operation, and to consider the pathologist's report on the faces to be sutured, lest excision of the neuroma has not been sufficiently radical. Our pathologist's forecasts from his sections have become less pessimistic as clinical results have been followed, and we believe that a certain firmness of the nerve-sheath which makes for easy and accurate anastomosis offsets a mild degree of endoneurial fibrosis, and that this matters more in the distal stump than in the proximal. Resection and resuture may also increase the anatomical dissimilarity between the apposed nerve-faces, and so introduce technical difficulty, as in the case of the change of shape of the median above the carpal tunnel.

Occasionally our results have been marred by the occurrence of tenderness at the site of anastomosis, even when a neuroma is hard, to detect by palpation. This is not incompatible with a good result as measured by return of power and sensation. It is apt to be most troublesome in those who react emotionally, or who have had few painful experiences, and therefore may be met with in patients of widely differing mental make-up. We believe that a conservative attitude is best in these cases, except when the neuroma is in or near the carpal tunnel, when free mobilization and early and persistent exercise of the fingers to keep their tendons free appear to give some relief. We feel that here, and here alone, there may be a field for the elaboration and provision of some protective covering around the anastomosis.

Sanders and Young have expressed the opinion that there is no need for resection and resuture of the distal anastomosis, to provide a fresh union for the transit of axons arriving from the proximal anastomosis. Experience in one case seems to substantiate this contention. A bomb-fragment struck the patient's left forearm while it was flexed at the elbow, emerged above the medial epicondyle and divided the ulnar nerve both at

its entrance and exit. He was operated on 101 days after being wounded. After re-section of all four neuromas, the intervening length of nerve, measuring 7·8 cm., was used as an autograft, the branches to flexor carpi ulnaris being sacrificed. Voluntary movement in the 5th slip of flexor profundus, which had been absent before, was noted 153 days after the suture.

Naturally re-exploration is required after preliminary bulb suture.

OTHER OPERATIONS TO IMPROVE RESULTS

It seemed to us possible that the motor and sensory results of suture of certain nerves might be improved if we reduced the total number of axons competing for tubes in the distal segment, by eliminating sympathetic fibres by performing a post-ganglionic sympathectomy on the limb, previous to the suture. Professor Seddon, with whom I discussed the matter, did not consider the reduction would be worth while; and we shall give the method only a limited trial. There is also the operation proposed by Dogliotti, in which a nerve is deliberately sectioned and resutured at some distance distal to the original anastomosis, in order to allow the axons to divide and increase. the number competing for distal tubes: would it be useful in the case of the median, after it has given off all its motor branches in the forearm? It appears from what Mr. Young has told us that the procedure might interfere with the maturation of the individual fibres. Finally, we believe that when the main artery of a limb has been divided as well as one or more nerves, before the downgrowth of axons reaches the digits a preganglionic sympathectomy should be performed, to prevent the reimposition of a degree of vasoconstrictor tone on the digital vessels.

Brigadier W. Rowley Bristow said he agreed in the main with Dr. Elkington's opening remarks, but thought he was perhaps unduly pessimistic and that patients tended to improve with more time. Most of the results of operation examined so far were inter-mediate results and not true end-results.

He advocated repair of a divided nerve as early as possible, that is as soon as the risk of sepsis had passed and exploration was to be regarded as safe from this point of view. A clean bullet or machine gun wound which had healed by first intention could be sutured within a week or two of the healing of the wound. Unfortunately many nerve injuries in war wounds were complicated by severe damage to other structures, e.g. fractures and joint injuries, and the healing process was prolonged and an unavoidable delay was imposed on the surgeon. It was therefore necessary to delay the operation on the nerve for some months, and the all-important consideration was to keep the muscles and joints of the paralysed member in as good shape as possible and free from contractures and deformity during this period

He gave it as his opinion that there was a tendency to over-splint the hand, both in the pre- and post-operative stage, and he disagreed with the teaching emanating from certain centres on this point, believing as he did that movement was the first essential in maintaining blood supply to the affected part. Discussing operative technique he stated that when a nerve injury was complicated by a malunited or an ununited fracture, the nerve should be explored before a definite operation on bone was undertaken, because bone shortening might allow of end-to-end suture, and bone shortening was not a formidable undertaking.

In his opinion, the findings up to the present time, were very similar to those seen in the last war and reported. He saw no evidence of any striking improvement either in methods or results, but there was a great improvement in recording and in note-taking under the M.R.C. scheme. This should make an end-result survey at a later date of considerable value.

Lt.-Colonel R. Glen Spurling, U.S.A.M.C., said that the Medical Department of the U.S. Army had, so far, made no provision for research in peripheral nerve injuries. However, the Surgeon General, Major-General Norman T. Kirk, had just recently directed that all patients with peripheral nerve injuries should be retained in the armed forces and given jobs commensurate with their disability until such time as they had reached maximum improvement. Further, each patient must report to the hospital where the last surgical treatment was given, for regular observation at intervals not to exceed ninety days. This directive should make possible a controlled system of follow-up obser-vations extending over a period of years.

An attempt had been made to contribute to the technical side of the problem by the use of very fine tantalum wire suture material, with a cuff of thin tantalum foil placed around the suture line. The foil was only used when the nerve must be replaced into a bed of scar tissue. It was believed that the foil cuff prevented fixation to non-mobile structures and the ingrowth of fibrous tissue at the suture line. Just how important this step might prove to be was as yet undetermined. Tantalum was certainly inert when buried in human tissue. It might be drawn into wire as fine as human hair and still retain excellent tensile strength.

His, Colonel Spurling's, experience with late sutures of nerves in battle wounds was discouraging in many instances because of the great gaps between the nerve ends. Many of the late problems could be simplified by better handling of the wounds in the acute stages. There was much to be said against primary nerve suture, yet he was sure

that if nerve ends were approximated at the original debridement with anything like reasonable care, later repair would be tremendously simplified. In some instances in fact, no secondary repair might be necessary because, after all, primary sutures were sometimes successful.

To minimize this retraction problem, they were instructing Army surgeons to bring severed nerve ends together when this could be accomplished without extensive dissection at the original debridement. If approximation was not possible then the nerve ends should be tacked down under tension to surrounding tissues to prevent retraction.

With the aid of chemotherapy it should be possible to do early secondary closures of the extremity wounds. At the Walter Reed General Hospital in Washington, during the past year, elective nerve surgery had been performed within two weeks after secondary suture of the wound. The incidence of serious wound infection had not been much greater than would have been expected in clean cases. Chemotherapy, both sulfa drugs and penicillin, had been used pre-operatively and post-operatively in all cases.

He was not in complete agreement with Professor Learmonth regarding surgical explorations. His policy had been to explore every case not showing definite evidence of improvement, as soon as circumstances permitted. Even after suture re-explorations were done if the signs of regeneration were too long delayed. Most operations were done with procaine infiltration anæsthesia, therefore, the risk of an exploration was negligible. Furthermore, the information obtained from electrical stimulation with the patient awake was most valuable.

Professor H. J. Seddon said that at the Oxford Centre they had found an appreciable difference in the quality of recovery of high sutures of the median or ulnar nerves as compared with sutures at about the level of the wrist (Dr. Elkington had mentioned that he had found little difference). Sutures at the wrist, if performed within nine months of injury, gave fairly good functional results, whereas high sutures of either the median or the ulnar nerves usually gave good recovery only in the forearm muscles but not in the hand. It was probable that poor results at the wrist were attributable to suturing the nerve with the joint in acute flexion. In a number of cases the subsequent correction of flexion produced serious damage at the suture line, sometimes amounting to complete separation. In order to obtain a good result it was essential to mobilize the nerve as high as the elbow, and to suture it with the elbow flexed to 90 degrees and the wrist in the neutral position or even slight extension. Post-operative stretching was carried out at the elbow—not at the wrist.

Professor Seddon agreed with all that had been said about the risk of stiffness after injudicious splinting, and the importance of maintaining mobility of a paralysed hand from the very first. But if it was realized that the aim of splinting in the treatment of nerve injuries was not immobilization so much as relaxation of the affected muscles, no harm—in fact only good—would result from the application of properly devised splints. It was true that at the Oxford Centre some sort of splint was applied in almost every case, but the apparatus recommended (Highet, 1942, *Lancet* (i), 555) permitted a considerable range of movement; in the median and radial splints relaxation was maintained almost exclusively by elastic bands that allowed the patient to use his digits freely. However, it was better to dispense with splinting altogether rather than run the risk of producing stiffness by rigid splinting and neglect of passive movements.

Professor Learmonth had advocated the use of pedicle grafts in cases where a large area of scar tissue lay over the site of division of a nerve, and there was no doubt that if nerve suture was to be performed a preliminary plastic operation was essential. Sometimes, however, the final operation—exploration of the nerve—revealed a gap too great to be closed and in such a case the whole purpose of the pedicle graft was lost; a split skin graft would have done just as well. Professor Seddon, therefore, recommended that the first stage of the plastic operation, namely, excision of the scar, should include exploration of the nerve. If it was found that the gap was too great to be closed by any means the stumps of the nerve should be buried and the more elaborate plastic operation abandoned in favour of the much less time-consuming split-skin grafting.

In answer to the President's inquiry about a system of grading of recovery after nerve lesions he drew attention to the system that had been approved by the Peripheral Nerve Injuries Committee of the Medical Research Council (*Bull. War Med.*, 1943, 3, 258). At the Oxford Centre it was in regular use and had been found fairly satisfactory.

Mr. J. E. A. O'Connell said he thought that Dr. Elkington's description of the prognosis in lesions of the common peroneal nerve was unduly pessimistic. His own series of peripheral nerve injuries was much smaller than that of most of those present but in it there was a group of common peroneal nerve injuries. In a fair proportion of cases good power in the peronei and dorsiflexors of the ankle had followed secondary suture of this nerve.

[*May 4, 1944*]

DISCUSSION ON DISORDERS OF PERSONALITY AFTER HEAD INJURY

Dr. Andrew Paterson: Personality is the pattern of behaviour which the individual exhibits in adjusting and reacting to his environment. It involves affective and dynamic factors including desires, drives, appetites, &c., and cognitive factors such as memory, perception and higher thought processes. These cognitive factors are harnessed—to use Sherrington's phrase—to appetites, drives and inclinations, so giving rise to a variety of interests and skills which vary from one individual to another.

Many neurologists and psychiatrists regard the personality of the individual as something quite apart from the functioning of the brain. In personality, the emotional and temperamental aspects of behaviour are artificially divorced from the perceptual and motor skills. This divorce has come about for a variety of reasons, one of the most important of which is the difference between the ways in which they are acquired. The cognitive and motor skills are well known to be evolved through a process of training and learning which is subserved by the brain, and certain of them, such as language, are taught in standard fashion and are also known to have a relatively well-circumscribed localization in the cerebral cortex. The similarity between the acquisition of a skill or special ability and that of the emotional and social personality pattern is overlooked. The training for the latter, though certainly essential if any adequate adjustment is to be made in ordinary life, takes place over a long period from an early age, is not standardized and to a large extent is unintentional and haphazard, in spite of the attempts of the English public school system. None the less, it is acquired. The emotional pattern of the child is modified and elaborated on the basis of past experience and this process is subserved by the brain. There appears to be less accurate localization of this aspect of human behaviour than might be desired—there appears to be no circumscribed cortical control such as is found in the case of motor phenomena and some sensory fields, though the loss of initiative and drive through severance of the frontal lobe tracts may indicate some ill-defined cortical influence. The absence of any well-circumscribed area of cortical control no doubt gives rise to the lack of fine discrimination and objectivity in regard to practical emotional settings and has given the philosophers an excellent ground for debating the standards of moral and social judgments and psychologists for the creation of abstract entities such as the super-ego, ego and id. There is no such controversy about the finer discriminatory judgments such as underlie speech and space perception. There is no setting up of psychic entities which control and make possible those abilities.

Personality as the individual pattern of behaviour, I shall then assume, embraces both cognitive and emotional attitudes and these are subserved at every step by the functioning of the brain.

The confusional state following head injury may be regarded as the acute breakdown of the personality pattern in many of its aspects. Its detailed study, although somewhat neglected in the past, we consider to be of supreme importance, not only because of the light which it may throw on cerebral functioning when it is impaired by trauma, but because out of this acute confusional state arises chronic personality change. The main characters of the latter may be thrown into relief and grossly exaggerated in the acute state and are therefore more easily picked up than in the chronic residual disorder. We all know how difficult it is to assess an old-standing post-traumatic case, especially when no history of the confusional state is available.

The term confusional state or confusion merits a few words of explanation. It is generally regarded as an alteration or impairment of consciousness, the latter being too often conceived as an entity apart from the individual functions which go together to form normal waking behaviour. It is an example of that inveterate tendency of the human to hypostatize abstractions so that they come to be regarded as real existent things in much the same way as external objects have an independent existence. The brain accordingly is thought of as producing consciousness in much the same way as the liver secretes bile. Just as the flow of bile can be diminished, so in certain states of the brain following injury we may have more or less consciousness, i.e. less or more confusion. This metaphor is obviously crude and false but there is another, more subtle though equally misleading. Consciousness is regarded as an inward light which can be switched from object to object as the need arises just as a physical beam of light can be switched. Confusion on such a view is regarded as the dimming of the light, and various phrases result such as clouding of consciousness, twilight state, &c. The dominance of visual perception in the ordinary waking state makes this metaphor of consciousness as a light extremely attractive but none the less misleading and to be avoided if we desire any better understanding of what consciousness means. If it is viewed as some sort of light, it would vary in intensity in one dimension. Some such idea, I feel, lies behind the findings of the psychological section of the Brain Injuries Committee when they describe confusion as divisible into 1st, 2nd and 3rd degree. Confusion so conceived would arise from generalized brain damage independent of the impairment of the individual focal functions, although these latter may be superadded as neurological features. This view of confus' . ives r:se to one of several artificial partitions between neurologists and psychiatri·· t ··· ˈ··· t time. Neurologists say of the confusional state that it is mental, is ä ɔ····ċ·n·ɾ··   ·· but they are prepared to study as neuro-

that if nerve ends were approximated at the original debridement with anything like reasonable care, later repair would be tremendously simplified. In some instances in fact, no secondary repair might be necessary because, after all, primary sutures were sometimes successful.

To minimize this retraction problem, they were instructing Army surgeons to bring severed nerve ends together when this could be accomplished without extensive dissection at the original debridement. If approximation was not possible then the nerve ends should be tacked down under tension to surrounding tissues to prevent retraction.

With the aid of chemotherapy it should be possible to do early secondary closures of the extremity wounds. At the Walter Reed General Hospital in Washington, during the past year, elective nerve surgery had been performed within two weeks after secondary suture of the wound. The incidence of serious wound infection had not been much greater than would have been expected in clean cases. Chemotherapy, both sulfa drugs and penicillin, had been used pre-operatively and post-operatively in all cases.

He was not in complete agreement with Professor Learmonth regarding surgical explorations. His policy had been to explore every case not showing definite evidence of improvement, as soon as circumstances permitted. Even after suture re-explorations were done if the signs of regeneration were too long delayed. Most operations were done with procaine infiltration anæsthesia, therefore, the risk of an exploration was negligible. Furthermore, the information obtained from electrical stimulation with the patient awake was most valuable.

Professor H. J. Seddon said that at the Oxford Centre they had found an appreciable difference in the quality of recovery of high sutures of the median or ulnar nerves as compared with sutures at about the level of the wrist (Dr. Elkington had mentioned that he had found little difference). Sutures at the wrist, if performed within nine months of injury, gave fairly good functional results, whereas high sutures of either the median or the ulnar nerves usually gave good recovery only in the forearm muscles but not in the hand. It was probable that poor results at the wrist were attributable to suturing the nerve with the joint in acute flexion. In a number of cases the subsequent correction of flexion produced serious damage at the suture line, sometimes amounting to complete separation. In order to obtain a good result it was essential to mobilize the nerve as high as the elbow, and to suture it with the elbow flexed to 90 degrees and the wrist in the neutral position or even slight extension. Post-operative stretching was carried out at the elbow—not at the wrist.

Professor Seddon agreed with all that had been said about the risk of stiffness after injudicious splinting, and the importance of maintaining mobility of a paralysed hand from the very first. But if it was realized that the aim of splinting in the treatment of nerve injuries was not immobilization so much as relaxation of the affected muscles, no harm—in fact only good—would result from the application of properly devised splints. It was true that at the Oxford Centre some sort of splint was applied in almost every case, but the apparatus recommended (Highet, 1942, *Lancet* (i), 555) permitted a considerable range of movement; in the median and radial splints relaxation was maintained almost exclusively by elastic bands that allowed the patient to use his digits freely. However, it was better to dispense with splinting altogether rather than run the risk of producing stiffness by rigid splinting and neglect of passive movements.

Professor Learmonth had advocated the use of pedicle grafts in cases where a large area of scar tissue lay over the site of division of a nerve, and there was no doubt that if nerve suture was to be performed a preliminary plastic operation was essential. Sometimes, however, the final operation—exploration of the nerve—revealed a gap too great to be closed and in such a case the whole purpose of the pedicle graft was lost; a split skin graft would have done just as well. Professor Seddon, therefore, recommended that the first stage of the plastic operation, namely, excision of the scar, should include exploration of the nerve. If it was found that the gap was too great to be closed by any means the stumps of the nerve should be buried and the more elaborate plastic operation abandoned in favour of the much less time-consuming split-skin grafting.

In answer to the President's inquiry about a system of grading of recovery after nerve lesions he drew attention to the system that had been approved by the Peripheral Nerve Injuries·Committee of the Medical Research Council (*Bull. War Med.*, 1943, 3, 258). At the Oxford Centre it was in regular use and had been found fairly satisfactory.

Mr. J. E. A. O'Connell said he thought that Dr. Elkington's description of the prognosis in lesions of the common peroneal nerve was unduly pessimistic. His own series of peripheral nerve injuries was much smaller than that of most of those present but in it there was a group of common peroneal nerve injuries. In a fair proportion of cases good power in the peronei and dorsiflexors of the ankle had followed secondary suture of this nerve.

[May 4, 1944]

DISCUSSION ON DISORDERS OF PERSONALITY AFTER HEAD INJURY

Dr. Andrew Paterson: Personality is the pattern of behaviour which the individual exhibits in adjusting and reacting to his environment. It involves affective and dynamic factors including desires, drives, appetites, &c., and cognitive factors such as memory, perception and higher thought processes. These cognitive factors are harnessed—to use Sherrington's phrase—to appetites, drives and inclinations, so giving rise to a variety of interests and skills which vary from one individual to another.

praxic and constructional components. These functions are in the main dependent on complex integration occurring in the parieto-temporal areas on both sides and they are more likely to be affected by a severe lesion than the relatively well-circumscribed area on one side which primarily subserves the correct execution of verbal tests.

I now come to the chronic or residual personality disorder. Some of the disabilities seen in the gross confusional state may fail to clear up completely, giving rise to relatively permanent changes constituting the post-traumatic personality change.

The most common cognitive changes are memory impairment, residual dysphasias and kindred symptoms and mild agnostic and apractic features. Some degree of intellectual deterioration is usually found. This is by no means the only important change, for, when present, the emotional component and the closely associated involvement of practical judgment are even more significant from the practical point of view. The term intellectual deterioration implies that there is a specific function called intelligence independent of the individual performances through which intelligent behaviour is expressed. Such a view of intelligence is analogous to the blanket term consciousness criticized above, and is open to exactly the same objections. Intelligence is measured by psychologists and expressed as an arithmetical figure, often as a percentage of the normal. The tests by which this figure is obtained are of a few arbitrarily selected capacities and presuppose a basis and background of perception and praxis which cannot be taken for granted in the case of brain damage. Indeed those tests which are called performance tests by psychologists are not tests of an imaginary entity called intelligence but assess the visuo-constructive ability of the individual, an ability subserved in very large part by the angular and supramarginal gyri on both sides. Visual constructive tests assess the functional efficiency of those parts of the brain in which the integrations underlying the appreciation of visual spatial relationships and their corresponding manual movements are built up.

Although undoubtedly of some value in the assessment of healthy individuals, no single battery of tests can adequately measure the variety and variability in the human adult with his specialized and highly developed interests and abilities, and when these tests are carried over by the clinicians and used for a purpose for which they were never originally intended, for assessing organic intellectual impairment, the position is very far from satisfactory.

Prior to the war the post-traumatic personality change had received scant attention and even scantier analysis. Under the stress of war, it has been necessary to find some quick method of assessing intellectual impairment and to distinguish the physiogenic from the psychogenic or, what I think is the proper dichotomy, the traumatic from the constitutional. On the outbreak of war there was a clamour for tests for intellectual impairment. The academic psychologists through no fault of their own were encouraged to produce tests for conditions of which they had little knowledge and no clinical experience. This is the very opposite of the clinical approach where close observation should lead to the formulation of a test. In no other sphere of clinical science are tests devised before the phenomena have been studied. Such tests devised *a priori* tie nature down to a certain pattern of breakdown and such an assumption has always hindered progress. It also leaves out of account the variety of ways in which interference with cerebral function may express itself in the field of performance. There is more than a danger that the stereotyping of modes of investigation will force us to think along those lines only, and to close our eyes to and cease investigation of the breakdown which the hard facts of clinical observation present:

Wechsler has found that in diffuse organic lesions the results on performance tests are relatively worse than those on verbal ones. The explanation is that the cortical functions which mediate performance on tests of this kind are various and depend on the integrity of those specific areas of the brain which subserve proper spatial localization and construction. As these areas are both bilateral and relatively extensive, it is only to be expected that performance test capacity is more likely to be involved in diffuse lesions such as occur in G.P.I. Even here, however, the stress may be focal as in Lissauer's paralysis. Wechsler finds his criterion of less value for cases of deterioration after head injury where focal impairments often fall on the speech areas, so selectively interfering with the score on verbal tests.

I should like to cite a case illustrating the difficulty in interpreting performance test scores particularly from the point of view of disposal. An engine driver, some time after a severe head injury, gave a low average on Kohs' blocks, although on other tests he reached average level. This suggested that he had some cognitive impairment. Does

logical entities the individual functions which are impaired. The psychiatrist finds himself at home with the confusional state, but throws up his hands and says "neurological" when any of the individual impaired functions come up for assessment, such as aphasia or some high level visual disturbance such as visual agnosia, but what could be more mental than these disturbances, and at the same time more neurological, arising as they do from lesions of relatively well-defined parts of the cerebral cortex?

Consciousness is nothing apart from the individual functions which can be distinguished in ordinary waking behaviour, perception, imagination, memory, speech, motor skills, emotional and social attitudes. As a commentator on Professor Jefferson's article on concussion in the *British Medical Journal* for January 1, 1944, stated, there are undoubtedly different modes of consciousness, or, as I would prefer to put it, different ways in which we are conscious or aware. Impairment of consciousness or confusion on this view would not mean merely a deficiency of a certain unitary, one-dimensional entity, but a variegated picture differing from one confusional case to another, according to the distribution of the contusional damage over the more or less circumscribed and in some cases localizable functions. I would maintain that the confusional state is always an individual affair to be studied as such, and not to be dismissed by the ignorant remark that one confusional case is very much like another. We base our evidence on daily verbatim records of what the confused patient says or does in response to a relatively standard type of interview, which has been built up on our experience of such cases. These verbatim records have been found to be imperative in studying the nature and in reviewing the course of the confusion.

For example, there are cases of confusion where visual agnosia is present and others just as "confused" where it is absent. Visual agnosia in such cases does not differ from that found in the more isolated syndrome.

A patient, during an acute post-traumatic confusional state lasting three months, failed to recognize his wife by aid of vision when she approached, although there was nothing the matter with his peripheral visual mechanism, and yet was able to recognize her voice. Here is an observation made during confusion which assisted in the localization of the main lesion and helped to forecast the nature of the residual impairment. In fact, on recovery, this man was found to have occasional difficulty in recognizing people well known to him, in judging distances and speeds, and in stepping on to a slowly moving vehicle. He was never able to learn his way round a new housing scheme in which he had subsequently gone to stay.

We have been interested in dysphasia arising in closed head injuries. In some cases there is not the slightest difficulty in naming objects. The paraphasic responses given in the confused state differ in no obvious way from those shown in cases of focal lesions without confusion, e.g. jargon aphasia and in the various stages of recovery.

Disorientation is regarded as the hall-mark of confusion, but we have found that its pattern, too, varies from case to case according to the main lesion. In a case recently studied it was found that in the course of reorientation the patient displayed a marked reduplicative paramnesia in respect of the hospital and his single room. He believed that he was changing from room to room and one hospital to another daily—always to a hospital rather like but not identical with the one in which he actually was. In a closed head injury he had a *contre-coup* lesion in the right occipitoparietal area, which as Holmes, Riddoch, Brain and others have shown, subserves the organization of visually perceived space. The failure to recognize a relatively large object such as a room is often shown in such lesions and this patient's reduplicative paramnesia had arisen on this basis. Again, when a patient makes gross mistakes in giving the correct year, it may appear that he has a severe temporal disorientation. We have found, however, that this is often dependent upon an acalculia, one of the mental disabilities with well-defined localization. Many similar analyses could be given showing that the more closely the confusional state is studied the more will its essential nature be seen to comprise impairment of a variety of functions and not of one imaginary entity called consciousness.

Further evidence in support of this view of confusion is provided by the differential way in which the various part functions are restored. For example, the disorientation and perceptual restriction may clear up before other disorders such as memory defect or emotional changes. This can be traced out if daily verbatim records are kept with a relatively standardized type of interview, such as I have indicated. It is also significant that the impairment on performance tests after the acute stage has passed is greater than that on verbal ones. Correct execution of performance tests depends upon the integrity of a number of co-ordinated functions visuo-spatial perception as well as

suade their M.O.s that they are fit and are discharged back to duty where their dis-
abilities may have serious consequences. Although just as ill as the anxious type they
are rarely recognized as such.

A study of the previous personality pattern is essential for an appreciation of the post-
traumatic emotional changes. Unlike the cognitive these cannot yet be assessed in a test
situation. · Only careful observation over some period and comparison with the previous
behaviour can give a clue to the disorder.

Major W. R. Reynell: Traumatic personality change following head injury is organically
determined. Any function of the mind, awareness, intellect, feeling or will may be altered
as well as the patient's morale—his attitude to his environment and to himself. Changes
of character, temperament, disposition and mood may be observed. Of all these changes
there is only one—intellect or the capacity to learn new tasks—which can be measured
with any degree of accuracy.

Neurological signs are usually absent and diagnosis may be difficult unless really reliable
information about the patient's previous personality is available.

No one of the above changes, except intellectual loss, can be said with certainty to have
been organically determined—it is the general clinical picture and history on which a
diagnosis is made and the interpretation may vary with the experience of the clinician.

It has long been recognized that intellectual impairment is the most significant and
serious finding in head injury cases—including those with personality change with which
it is usually associated—but assessment of such impairment has often been arrived at
on clinical grounds alone, with rough and unstandardized tests of memory, calculation
and general information.   The validity of psychometric testing for the presence of
intellectual loss has been established by the work of Wechsler, Babcock, Shipley, Brody,
Conkey and others and does not involve writing to unknown persons concerning the
patient's previous abilities—valuable as such information may be when obtained from a
reliable source.

It is well-known that certain functions of the intellect are more vulnerable than others
and tend to fail first in cerebral disease and injury—as in the ageing process. For this
reason differential testing can be used as an index of intellectual impairment and yield
information of value in assessment and prognosis, besides giving an objective record of
progress of great value to the clinician and help to the patient, who often becomes immune
to mere encouragement when he knows that he has suffered a loss of capacity.

It has been found that patients with severe cerebral damage—whether due to abscess,
tumour or trauma—show in almost all cases large discrepancies on differential testing as
do those with grossly abnormal air encephalograms.

On the other hand psychoneurotic cases rarely show differences of the characteristic
"organic" pattern when the results of tests, perceptual and conceptual, verbal and per-
formance, are considered as a whole.

I have now tested more than 1,500 cases of head injury with psychometric tests but
the results have been followed up in the first 500 only. Cases showing intellectual loss,
two months or more after injury, carry a much worse prognosis as judged by the per-
centage invalided on general clinical grounds (80% of the first 100 cases)—in the propor-
tion of 4:1—than those with injuries of similar severity who showed no such loss (of 100
cases 80 were returned to duty). It seems clear that psychometric findings are a valuable
"pointer" in prognosis.

In considering cases of undoubted traumatic personality change I have found that only
a small proportion fail to show evidence of intellectual loss on careful psychometric test-
ing—actually 6% of the last 50 cases examined, of whom 25 were N.C.O.s and 6 were
officers. No less than 47 showed evidence of intellectual loss on full testing, 45
showed a "positive" result on a differential test—i.e. a difference of 10 or more between
the I.Q.s corresponding to two series of tests, the first of vocabulary, general information
and comprehension which "hold up" well and the second of arithmetical reasoning, digit
retention—forwards and backwards, and similarities—which do not "hold up" well.
Forty-eight of these cases showed retardation on performance tests and 46 showed dis-
proportionately low scores on Raven's matrix — compared with those on vocabulary,
general information and comprehension.   Thirty-eight showed impaired memory for
words, shapes, or patterns and 35 showed a poor "learning curve" on the Rey Davis
board.

this observation help in deciding whether or not this man is fit to resume his usual work? Taken by itself it does not. It indicates only that more precise investigation of impairment in the visual-constructional sphere is required. Even when this has been done, however, it is only by thorough inquiry in many fields, not by any means all of which can be studied experimentally, that the practical significance of the impairment can be assessed. In this case further analysis showed that he was bad at judging distances and speeds and therefore unfitted for work as an engine driver. He had an atrophic lesion in the right occipito-parietal area.

The uncritical use of tests—even tests of special aptitudes such as arithmetic—may be positively misleading. Thus we have seen at least two cases who attained entirely normal standards on the Wechsler and other tests of mental arithmetic, though displaying gross impairment of sustained mechanical arithmetic such as simple routine addition. In this connexion, I should like particularly to stress an aspect of impairment which may be loosely called cognitive inefficiency. The majority of mental tests in common clinical use are particularly ill-adapted to bring out this important quality of impairment. In brain-injured cases there is very commonly an abnormal inconstancy of response. While nine times out of ten they will give a correct answer or perform a correct action, every now and again for no obvious reason they fail completely. This inconstancy is akin to the fluctuations in sensory threshold judgment which Head and Holmes found in lesions of the parietal lobes. It can also be linked up with the inconstancy of the emotional response in brain-injured people giving rise to the characteristic combination of apathy and lability. In short, this disability is a failure to maintain a uniform standard of response. The proneness to early fatigue in such cases is an important factor in this inconstancy.

Zangwill has emphasized that learning is very commonly impaired in the post-traumatic personality change and that this function is assessed, if at all, only incidentally by test batteries such as that of Wechsler. We frequently find that these patients are unable to learn new jobs, new processes, or even to revise old ones. Proper study of learning and the adaptation, where possible, of tests specially designed to assess its impairment are thus of considerable practical importance.

I will now briefly refer to the emotional aspects of the post-traumatic personality disorder. During the development from child to adult the normal individual acquires a relatively permanent and stable pattern of emotional response; interests and desires are adjusted to the varied aspects of his social environment. This balance is reached by the constant action of standards of social and moral requirements and restrictions. After head injury this balance is upset. The emotional response becomes maladjusted and inconstant, not controlled by its previous standard. In Symonds' phrase, the individual becomes less of a man and more of a child. As I have pointed out elsewhere, in the acute confusional state emotional responses are often isolated, excessive and act for an unduly long time, suggestive of the decorticate response in animals. When the confusion clears and the emotional pattern returns to something like its previous state we often find an exaggeration of the dominant emotional traits which the patient previously exhibited, together with a fixity of attitude, a lack of plasticity. We have found that the majority of the post-traumatic emotional changes fall into two groups—excessive fear and anxiety on the one hand, and euphoria and aggression on the other. These are only general tendencies and do not imply that the individuals are always aggressive or always anxious. Other responses occur of course, one towards suspicion and also the quite common one where there appears to be diminution or blunting of all emotional reactions. Possibly because fear is such a basic, useful and self-protective instinct we have found that a high proportion of emotional disturbances are of the anxious type. A fear response is accentuated by looking back on the setting of the accident. On coming to himself in strange surroundings, the brain-injured man is emotionally impressionable and anxiety has greater opportunity of showing itself, the lack of plasticity in changing the mood enables it to outlast its usual period.

On the other hand there are some people whose dominant mood is extraverted and aggressive and to whom the war setting is almost congenial. Following head injury these individuals show an exaggeration of these characteristics and in this excessive response demonstrate as much maladjustment as does the anxious type. The difference, however, is that in the case of the apprehensive type the patient is acutely aware that he is different and in some way ill: the very nature of the euphoria in the other type precludes such insight. Far from regarding himself as ill he believes that he is better and more efficient than before. He does not recognize a possible mood change and memory retention defect and tends to gloss over and ignore failure. Such people per-

found to be significant of intellectual loss in a great majority of cases which have subsequently been tested more fully by Kohs' blocks, digit symbol, matrix, Rey Davis board, Babcock's sentence and other memory tests; and if thought necessary by Test 33 of the National Institute of Industrial Psychology, Cattell's test Form A and B—or other tests which seem most applicable.

Twenty-five per cent. of 800 cases referred for testing two months or more after head injury showed indications of intellectual loss both clinically and psychometrically with an average difference of 14 in the I.Q.s corresponding to the A and B series—of those followed up (60%) 80 out of 110 were discharged from the army and 80% of an equal number with moderate or severe head injuries but without such evidence of intellectual loss were returned to duty. These disposals were made on clinical grounds alone and not on the results of tests. The chances of such a result being fortuitous are, I am told by a statistician, less than one in a million.

Of a control group of 50 psychoneurotic cases, 46 gave negative results on differential testing. The average weighted scores of 150 deteriorated cases were 11·9, 11·1, and 12·1 for the A series and 9·8, 8·4, and 9·9 for the B series—showing that the latter all tended to hold up badly.

The most constant finding was a falling off in performance tests, especially Kohs' blocks. This agrees with the results of Goldstein, Wechsler, Conkey and others.

Impairment of the "abstract approach" in Goldstein's phrase, was very characteristic: shown by poor scores on similarities, analogies (Test 33) and other tests of conceptional or "relational" thinking. A degree of acalculia was very common and striking in patients who had previously been good at figures. If a patient stated that he had always been "hopeless at arithmetic" an alternative test—e.g. a performance one—was substituted in the B series.

Difficulty in repeating digits backwards was very frequent. Thus 100 deteriorated cases, excluding those "dull and backward" gave an average of 4·2 digits backwards, 50 "dull and backward" patients gave an average of 4·0, 50 psychoneurotics 5·3 and 50 "normals—excluding those dull and backward" gave an average of 6·2. Thus it would appear that if a patient can repeat only 4 digits reversed he is probably dull and backward or has suffered intellectual loss. Wechsler arrived at the same conclusion.

Intellectual abilities are of such variety and complexity that it is impossible to devise a battery that will assess all of them, and for practical use the method must not be too time-consuming. Nevertheless the A and B series of tests supplemented by observation during performance tests enable one to investigate a considerable number of faculties— e.g. memory, recent and remote, auditory and visual, verbal and non-verbal; synthetic and analytical capacities; reasoning and abstract thinking; comprehension, initiative, and judgment; the four fundamentals of arithmetic (addition, subtraction, multiplication and division); dysphasia; visual imagery; constructive ability and speed—any or all of which may be impaired in post-traumatic states.

The best test of impaired capacity would be a man's ability to do his former work and to learn new forms of skill in comparable conditions, but opportunities for such a test are rarely available, and many factors, such as loss of confidence, regression, and results of hospital life, make it difficult to reconstitute the *status quo ante* after a severe head injury. We must do the best we can with the information derived from notes available and the personal interview. The results of psychometric testing will usually give valuable aid in the final assessment.

The A and B series of tests can be given in 20 to 30 minutes by a psychiatrist with experience of mental testing. The results will, of course, depend to some extent on the skill and experience of the user. This personal factor is inherent in all clinical tests and does not apply to psychometry alone. About 10% of cases with clinical evidence of intellectual impairment may fail to give a positive on such a differential test, but in these cases further and more time-consuming tests will usually establish the presence of impairment.

About 80% of head injury cases of all degrees of severity will show no clinical evidence of intellectual loss, and in these cases a negative result on the A and B series will support a favourable prognosis arrived at on general clinical grounds. Similarly, psychometric evidence of intellectual impairment—the most significant of all findings in head injury cases—will give weight to an unfavourable prognosis indicated by general clinical assessment.

It may be difficult to describe in words how much efficiency has been impaired, but if

Acalculia, poor scores on Kohs' blocks and impaired "spatial" sense were frequent findings.

Although 9 out of 10 cases with personality change showed evidence of intellectual loss the reverse was by no means true. A majority of cases with intellectual impairment showed no striking personality change. There was often an awareness of lowered capacity and some apprehension about ability to perform their duties if returned to service, and such men are doubtful risks, liable to develop anxiety states if returned to duty.

The percentage of cases showing intellectual loss will, of course, depend on the severity of the change in total personality, and in all these 50 cases the change was marked and had been noted by the patient's C.O., wife, relatives or close friends.

The correlation between such changes and intellectual loss is evidently high but there are, of course, cases in which the intellect is spared.

The intellectual functions may show impairment in loss of speed, in memory—verbal or non-verbal—visual or auditory, in calculation, reasoning capacity, abstract thought, visual imagery, spatial sense, constructive abilities or in learning capacity. Awareness may be increased with poorly sustained attention, irritability, restlessness, insomnia and fatigue.

Whatever the nature of the intellectual loss it will be shown by a suitable battery of psychometric tests which will show disproportionately low scores in one or usually in several of such tests—the results will be compared so far as possible with the man's previous abilities. If a good arithmetician now has acalculia; a man with a good memory for words, faces, direction and spatial relationships may now be defective in such abilities; a good examinee may fail badly in "abstract" tests; a carpenter or mechanic may do badly on block design—all such findings are significant and will reinforce a diagnosis of traumatic personality change arrived at on general clinical grounds—similarly the absence of such findings will reinforce a more favourable prognosis in many cases and suggest that the affective changes may be temporary. The frequency of the association of intellectual impairment and personality change is so great that finding of such loss may be considered a "sign"—so commonly present as to be significant although, like other clinical signs, it is not necessarily present. So frequent has been this association in the cases I have examined that I must confess that a case diagnosed as personality change in absence of intellectual loss is to me somewhat suspect—although undoubtedly such cases do occur.

While it is true that personality is a complex of related abilities and feelings which may be broken up by cerebral injury, the extent of the damage may be assessed more accurately if it can be found which faculties are more or less intact and which are severely impaired. Intellect, awareness and feeling may all have suffered but the first of these is the only one which can be measured. Alterations in will and feeling will often be revealed during testing more clearly than in a face-to-face interview when self-consciousness and inhibitions may be more in evidence. The process of testing is in itself a valuable psychiatric interview and much may be learnt, not only about the extent of the disability but the nature of it—i.e. whether it is due to neurosis or dementia. A marked discrepancy between scores on perceptual compared with those on conceptual tests points strongly towards intellectual impairment whereas neurotic behaviour and uneven scores on all tests suggest affective disorder.

It is not suggested that psychometric testing is a short cut to assessment, which must always be made from a consideration of the whole clinical picture but such tests help in distinguishing between incapacity which is due to neurosis and neurosis which is the result of incapacity.

Where a large number of cases has to be investigated it saves times to use a differential test as a "sieve" with a mesh fine enough to catch the great majority of intellectually deteriorated cases, yet rapid enough for practical use. Cases so separated are then subjected to such further testing as may be necessary to establish the diagnosis of intellectual loss and the nature of it.

For the preliminary differential test I have selected six tests from those described in Wechsler's "Measurement of Adult Intelligence." The first three of these tests, which I have called the A series, consist of vocabulary, general information, and comprehension, all of which "hold up" well in cerebral injury or disease; and the second three—the B series—are arithmetical reasoning, digit retention (forwards + backwards) and similarities —all of which tend to fail rapidly in traumatic intellectual loss. If the I.Q. corresponding to the scores in the A series exceeds that indicated by the B series by 10 or more the test is considered "positive". This figure is an arbitrary one but it has been

found to be significant of intellectual loss in a great majority of cases which have subsequently been tested more fully by Kohs' blocks, digit symbol, matrix, Rey Davis board, Babcock's sentence and other memory tests; and if thought necessary by Test 33 of- the National Institute of Industrial Psychology, Cattell's test Form A and B—or other tests which seem most applicable.

Twenty-five per cent. of 800 cases referred for testing two months or more after head injury showed indications of intellectual loss both clinically and psychometrically with an average difference of 14 in the I.Q.s corresponding to the A and B series—of those followed up (60%) 80 out of 110 were discharged from the army and 80% of an equal number with moderate or severe head injuries but without such evidence of intellectual loss were returned to duty. These disposals were made on clinical grounds alone and not on the results of tests. The chances of such a result being fortuitous are, I am told by a statistician, less than one in a million.

Of a control group of 50 psychoneurotic cases, 46 gave negative results on differential testing. The average weighted scores of 150 deteriorated cases were 11·9, 11·1, and 12·1 for the A series and 9·8, 8·4, and 9·9 for the B series—showing that the latter all tended to hold up badly.

The most constant finding was a falling off in performance tests, especially Kohs' blocks. This agrees with the results of Goldstein, Wechsler, Conkey and others.

Impairment of the "abstract approach" in Goldstein's phrase, was very characteristic: shown by poor scores on similarities, analogies (Test 33) and other tests of conceptional or "relational" thinking. A degree of acalculia was very common and striking in patients who had previously been good at figures. If a patient stated that he had always been "hopeless at arithmetic" an alternative test—e.g. a performance one—was substituted in the B series.

Difficulty in repeating digits backwards was very frequent. Thus 100 deteriorated cases, excluding those "dull and backward" gave an average of 4·2 digits backwards, 50 "dull and backward" patients gave an average of 4·0, 50 psychoneurotics 5·3 and 50 "normals—excluding those dull and backward" gave an average of 6·2. Thus it would appear that if a patient can repeat only 4 digits reversed he is probably dull and backward or has suffered intellectual loss. Wechsler arrived at the same conclusion.

Intellectual abilities are of such variety and complexity that it is impossible to devise a battery that will assess all of them, and for practical use the method must not be too time-consuming. Nevertheless the A and B series of tests supplemented by observation during performance tests enable one to investigate a considerable number of faculties— e.g. memory, recent and remote, auditory and visual, verbal and non-verbal; synthetic and analytical capacities; reasoning and abstract thinking; comprehension, initiative, and judgment; the four fundamentals of arithmetic (addition, subtraction, multiplication and division); dysphasia; visual imagery; constructive ability and speed—any or all of which may be impaired in post-traumatic states.

The best test of impaired capacity would be a man's ability to do his former work and to learn new forms of skill in comparable conditions, but opportunities for such a test are rarely available, and many factors, such as loss of confidence, regression, and results of hospital life, make it difficult to reconstitute the *status quo ante* after a severe head injury. We must do the best we can with the information derived from notes available and the personal interview. The results of psychometric testing will usually give valuable aid in the final assessment.

The A and B series of tests can be given in 20 to 30 minutes by a psychiatrist with experience of mental testing. The results will, of course, depend to some extent on the skill and experience of the user. This personal factor is inherent in all clinical tests and does not apply to psychometry alone. About 10% of cases with clinical evidence of intellectual impairment may fail to give a positive on such a differential test, but in these cases further and more time-consuming tests will usually establish the presence of impairment.

About 80% of head injury cases of all degrees of severity will show no clinical evidence of intellectual loss, and in these cases a negative result on the A and B series will support a favourable prognosis arrived at on general clinical grounds. Similarly, psychometric evidence of intellectual impairment—the most significant of all findings in head injury cases—will give weight to an unfavourable prognosis indicated by general clinical assessment.

It may be difficult to describe in words how much efficiency has been impaired, but if

testing shows a performance say 15% below the average and perhaps 30% below what would be expected from the score on the A series, we have some measure of the damage sustained. Furthermore, we have in such figures a standard by which to assess improvement should this take place, thus providing a record of progress which is encouraging to the patient and an aid in treatment. It is not claimed that such a difficult matter as assessment of post-traumatic personality impairment can be reduced to the comparative simplicity of psychometric testing, but in many cases it is difficult to arrive at a just assessment without the aid of such tests.

The criterion of a good test is that it should show a high correlation with the total score. The results of psychometric testing, taken as a whole, show a high correlation with the total clinical picture.

Major Michael Kremer: In spite of the work continually being done on the subject of disorder of the personality following head injuries there is still considerable confusion and disagreement about the manifestations. On going through the notes of 2,700 cases of head injury admitted to a military hospital recently, I was struck by the disagreement which existed between the most competent observers as to the presence or absence of personality disorder in a particular case.

Stated in bald terms the problem appears simple but in actual practice it is not so. In hospital and in the Services generally the assessment of the pre-traumatic personality is usually made by taking a personal history from the patient. This is faulty because: (1) Few patients are any good at real self-analysis—particularly the less literate. The patient tells what he thinks he is like—the less pleasant details are genuinely suppressed. (2) It is perforce taken after the injury—when the patient is quite often lacking in insight. An account from a relative is really what is required—if possible not a blood relation because these often have the same taints as the patient and so are blind to them. I have read letters from parents and brothers who have been described as stable yet who from their correspondence are obviously psychopaths. A wife—a sensible wife—will probably give a better account of a man than anyone else. But even this may be faulty because the life described may have been so sheltered that one just does not know how that person would stand up to the buffetings of a harder existence. We have all seen the individual who has fallen into a groove sort of job: who has been protected first by his mother and then by his wife, and who superficially is apparently settled and stable. When he is pitchforked into the Service and has to fend for himself he promptly develops an anxiety state. A rapid personal history taken from such a man before his breakdown could not reveal whether or not he would stand up to difficulties. There is no means of telling. We must acknowledge the possibility of breakdown and perhaps label this man as a non-aggressive personality but further than this it would be impossible to go.

Having assessed as best we can the pre-traumatic state we come to the crux—what is the individual like now, after the accident? The figures I obtained from the first thousand cases have naturally had the longest follow-ups but so far the figures are much the same for the next 1,500. The number that were considered to have a personality disorder by almost every one who saw them was 58. Because of the uncertainty it is not strange to see that these cases were the more severe: all had gross changes which persisted for over three months after the end of the post-traumatic amnesia. Almost all had changes which persisted very much longer than that. If one uses the length of post-traumatic amnesia as a criterion of the severity of the injury—and while this appears to me sound I am by no means so certain that the brevity of the post-traumatic amnesia indicates the relative insignificance of an injury—then it appears that personality change is related to the severity of the damage; the figures go like this:

P.T.A.	Total number of cases	Number and % of cases with personality change	Number and % of cases invalided	Number invalided for personality changes		% cases with personality change (invalided)
				From hospital	Later	
None	96					
Less than 1 hour	195					
1 to 24 hours	285	6 (2%)	123 (43%)	1	3	67%
1 to 7 days	228	15 (7%)	101 (44%)	5	6	73%
More than 7 days	156	37 (24%)	93 (60%)	16	18	92%

(Based on Symonds, C.P., and Russell, W.R., 1943, *Lancet*, i, 7.

In the personality change groups I have not included cases which, though showing this change, would have been invalided because of a severe physical disability—nor have I included the epileptics. It is quite obvious that the outlook for these cases as far as Service is concerned is bad. Sooner or later they will have to be sent back into civil life.

Here their outlook is very little better. For whatever reason it be, and I have carefully excluded the cases with real physical incapacity, these men do not make a very good showing even in civil life. Most of them can do only the simplest jobs even with careful nursing by their employers and relatives. They appear to be unable to hold their jobs, often because of the associated intellectual impairment, but often also because their irritability or apathy makes them impossible employees. To illustrate this:

A man aged 29—previously of quiet cheerful temperament—had a closed injury with a post-traumatic amnesia of four days. He had a C.S.F. rhinorrhœa which was dealt with by an early plastic operation. Three months' attempted rehabilitation was tried. Following this—with an optimism which few of us would have now—he was sent back to duty. Commanding Officers and senior N.C.O.s found him difficult, intolerant of discipline and aggressive. Other men in the same unit could not get on with him and after two changes of unit he was sent back to us nine months after the accident and was invalided. For the next two years he went from job to job, never staying in any one for more than three months. We have illuminating letters about him from his wife—an ex-nurse—who is a most sensible woman, describing his attempts and his failures to adjust himself to working for others. The situation has apparently been saved by the death of his wife's mother who left them not only a little money but also a car and he has now become a private-hire taximan. Since he has been doing this and working for himself he says he is much improved and much more settled. His wife, however, feels that there has been no fundamental change but merely that he can work when he feels so inclined and that he does not think he is being ordered about by anyone. It is only constant care by his wife and the fortunate legacy that has enabled this man to achieve anything like a reasonable existence.

As to the nature of the changes which occur: about two-thirds of our cases showed disinhibition, increased irritability and suspicion—easy annoyance and bad temper—sometimes going on to explosive rage. This may be associated with euphoria though the latter is more often accompanied by a silly fatuousness, garrulity, or childishness and irresponsibility. The other large group comprises the apathetic individuals with diminished initiative and apparently poverty of affect. Only in four cases have we records of social offences following injury. One was arrested for indecent exposure and three for stealing. I have only the patients' word to suggest they were not addicted to this prior to the head injury. Obviously any combination of the changes I have mentioned is possible and I have not found any relation between the severity of the injury and the nature of the disorder. I have not met a case in which the personality was changed for the better. Even when the patient thinks he is a better man his relatives are by no means certain, and often when the patient has left the hospital and is questioned later he admits a disability. One or two cases have thought they were improved by being quietened down from daredevils but this usually means they have had their drive literally knocked out of them.

A typical case. A captain aged 29, a regular officer, was admitted to the hospital in March 1941 a few days after a motor-cycle accident. He was bleeding from the nose and the right ear. He was very drowsy on admission and had a global dysphasia. He had fissure fractures in both parietals running into the middle fossæ on both sides. He remained confused for fifteen days and there was visual agnosia and dysphasia for three to four weeks. He improved fairly rapidly and the electro-encephalogram which had been grossly abnormal at first was almost normal in the middle of July. C.S.F. examination and air encephalography were normal. At this time he was very fit and free from headache and he had no trace of dysphasia apart from occasional spelling mistakes. It was questioned whether memory and intellectual ability had properly returned to normal. He was returned to duty in Category A. Since return to duty he has been in about fifteen jobs and his category has been lowered by successive medical boards until he was in Category C. He has been working in a variety of units including one with a most friendly and understanding C.O. who knew him before the accident. He was unable to stand up to any of them. He complains that he cannot concentrate, that his mind gets in a whirl and that "things fly at each other in his mind." He finds that he is lacking in initiative, has difficulty in making decisions and because of this he is not nearly so good a leader as he used to be. He is lacking in ideas and is too lazy to take action to bring about changes which he realizes are necessary. He cannot mix well and is very conscious of his difficulty in making conversation; he dreads dealing with senior officers, dislikes responsibility and would not take promotion if it were offered to him. Since his accident he has had five attacks of depression. His remote memory is good but he is forgetful now when he has to remember several things at once. His wife, when interviewed, confirmed all these points and made it quite clear that he was now a very different man from the pre-traumatic state and that his efficiency was considerably impaired. He was invalided.

Sometimes a change in personality may not be recognized until the patient has left the hospital and has to face the outside world.

This is well seen in the case of a lieutenant who had a moderate head injury resulting in a post-traumatic amnesia of four days. He made an apparently good recovery and after a period of rehabilitation he was returned to duty in Category A. When he was followed up at the end of the year he was reported as doing full duty efficiently and willingly at his depot. The second follow-up showed that he had gone abroad and he

was put down as a continued full recovery. It was only by chance that the medical officer who had looked after him in the hospital was posted to the same part of West Africa. They were both admitted as patients to the same hospital and so the M.O. was able to make a close study. He found that this apparently fully recovered head injury was feckless, unreliable, and incapable of sustained concentration or attention. When telling me of this case he said it was only when one lived with this sort of patient that one could see his defects. The patient could barely recognize them his insight was so defective.

The association with intellectual impairment is very frequent but this is to be expected because it is also a feature in cases with a long post-traumatic amnesia. There is, however, no parallelism. Cases can be seen in which it is impossible to detect any real intellectual defect by any battery of tests, and yet who have obvious personality change as seen by the relatives. The reverse is I think also true but by no means so easy to recognize. Probably intellectual defect is present in every case but our means of recognition are too coarse to detect it. The gross changes in personality we all recognize quite easily but there must be every gradation from the most minor to the most severe and it is only in the minor ones that help is needed in order to make a diagnosis. The presence of intellectual impairment makes one very suspicious but the real help comes from someone who has lived in intimate contact with the patient before the accident. Often they can point quite definitely to characteristics that have altered—things of which the patient is quite unconscious and which the doctor can only suspect.

Finally, there is that group of patients who manifest the change by the production of what appear to be psychoneurotic symptoms. We know that diseases affecting the cerebrum such as encephalitis lethargica can produce a symptomatology indistinguishable from any affective disorder in the predisposed. A head injury may do exactly the same. If an individual will produce the same reaction to a head injury as he would to his girl friend throwing him over, or an attack of influenza or breaking his leg, then the neurosis can only be post-traumatic in a chronological sense. If, however, the head injury changes a stable individual of stable stock into one who can no longer adjust himself to the stresses and strains of life, and to the stresses and strains produced by his own disabilities then I feel the neurosis is post-traumatic in an ætiological sense and is therefore a true personality change. In most cases the problem is not at all simple or clear-cut and all too frequently the pathogenesis is mixed. My reason for raising this point is that I have frequently read as a comment on a case that the patient is suffering from a psychoneurotic reaction to his head injury, when a more correct interpretation would have been that because of his head injury the patient's personality is now such that he develops a psychoneurosis.

Section of Odontology

President—HAROLD CHAPMAN, L.D.S.Eng.

[*April* 24, 1944]

Vincent's Ulceration: The Problem of Persistent and Recurrent Infection

By A. FRANK STAMMERS, B.D.S.Birm.

IT is well known that during the war years Vincent's infection has been prevalent among the civil population of this country, especially in industrial centres, as well as in the Armed Services. At the Birmingham Dental Hospital I have had the opportunity of examining and treating a large number of these civilian cases, and my recent publication in the *British Dental Journal* (1944) gave some facts and figures regarding 1,017 cases seen during the period June 1941 to December 1942. From that date to the present time—a period of sixteen months—between 1,400 and 1,500 additional cases have been registered and details of treatment recorded, but the results have not been tabulated. Nevertheless, I can state quite definitely that in general the findings recorded in the first series have been fully confirmed and in some respects amplified.

In the absence of full tabulated results for the new series of cases Table I gives the general results of treatment of the previous series.

TABLE I.

COMPLETED CASES		UNCOMPLETED CASES		
No Recurrence	Recurrence	No Recurrence		Recurrence
		Infect: cured	Infect: not cured	
	Once 14 Twice 1 3 times 1			Once 78 Twice 36 3times 9 4 · 4 10· 1
·538	Total 16	121	214	Total 128
	Eventually cured – No recurrence			
63				
Total 601				

This shows the number of recurrent cases related to "Completed" and "Uncompleted" treatment. A period of four months had elapsed from the date of admission of the last patient, and twenty-two months from the date of admission of the first patient of the series when this table was compiled. During the twelve months from that time to the present only about ten of these patients have returned with a recurrence of infection and most of those belonged to the "Uncompleted" group. While it is realized that some patients may have left the district or sought treatment elsewhere it is believed that their number would not materially affect these collective results or the conclusions arising therefrom.

"Completed" treatment implies not only the healing of all Vincent's lesions—clinically estimated by re-epithelialization of the ulcers and no bleeding on pressure—but also the removal of pockets and other stagnation areas.

AUGUST—ODONT. 1

Cases which were unnecessarily prolonged because of brief interruptions of treatment are not classed as recurrent.

No real significance regarding treatment can be attached to the group of 335 cases, i.e. Uncompleted—no recurrence. It may be assumed that a fair proportion of the 121 with healed lesions are still free from infection. On the other hand all of the 214 with un-healed lesions when they ceased attendance must be considered to retain a subacute or latent infection. However, this latter group does give some indication of the number of people whose mouths are in a dangerously unhealthy condition for which they do not seek treatment until subjective symptoms become acute. Most of the cases of ulceration and infected sockets following recent extractions can be accounted for by the failure of dental practitioners to recognize this subacute or latent infection and to give appropriate pre- and post-operative treatment.

A comparison of the number of recurrent cases in the two main groups—16 out of 617, i.e. 2·6% after complete treatment, against 128 out of 463, i.e. 27·6% after incomplete treatment—is very significant.

The 16 recurrences after complete treatment, all demonstrated the great importance of local conditions in favouring reinfection. Most of them had completely neglected oral hygiene and six were heavy smokers, i.e. thirty or more cigarettes a day.

The number of patients who ceased attendance before completion of treatment and returned because of a flare-up (50 of them more than once) gives an indication of the difficulty of treatment when control cannot be exercised or disciplinary measures taken.

From the comparison of these figures it will be seen, therefore, that the solution of the problem of recurrent infection lies in the complete eradication of all stagnation areas. In many cases this treament becomes complicated and delayed by persistent subacute ulceration.

Control of the acute stage is quite simple and straightforward. Latterly, therefore, attention has been focused mainly upon persistent cases and an attempt has been made to assess the causative factors involved and to accelerate cure.

It was found that only a small proportion could be considered to be really atypical.

A few were associated with pregnancy, with ulceration superimposed upon pre-existing gingivitis gravidarum. In only one such case was it considered advisable to excise the gum flaps, and the result was excellent. In the other cases healing of the ulcers was delayed, and the gingivæ were still inflamed and bled on pressure when the patients were discharged. They were given careful instructions regarding home treatment and were told to return if there was any deterioration of the condition.

Some patients with persistent lesions proved to have a positive Wassermann reaction. These responded well to local application of arsenicals in addition to general antisyphilitic treatment. In all probability many cases which have responded uneventfully to routine treatment have also had unsuspected syphilis.

A few cases were very intractable until vitamin therapy in addition to local measures was employed.

There were a number of cases from which smears were obtained showing that a heavy mixed infection persisted after the bulk of fusospirochætal organisms had been destroyed.

Finally some mouths exhibited marked anatomical abnormality, such as exceptional protrusion of the upper incisors or great crowding in the lower incisor region. These proved very stubborn owing to the impossibility of preventing mouth breathing, or of keeping zinc oxide and oil of cloves packs firmly in place. The prognosis in these cases was generally poor.

However, *the most frequent cause* of delayed healing was found to be simply the failure on the part of either the patient or operator to carry out certain essentials of treatment.

ON THE PART OF THE PATIENT

Failure to attend regularly.—This is the chief difficulty attendant upon the treatment of hospital out-patients.

Lack of co-operation in carrying out home treatment including persistence in smoking.—Experience has shown that demonstrations and verbal instructions are not always sufficiently impressive, and now in addition to these, a printed slip giving precise and strict instructions is issued to each patient.

ON THE PART OF THE OPERATOR

Failure to treat all parts of the mouth at each visit.
Hasty packing with zinc oxide and oil of cloves paste resulting in loose dressings.

Section of Odontology

Delay, sometimes unavoidable, in completing extractions, gingivectomy, &c.; and failure to continue prophylactic treatment in the interim.

Failure to check instructions previously given.—Instances have been recorded when the patient has been told to stop brushing the teeth during the acute stage and then not told when to start again. Repeated checks should be made to be sure correct instructions have been *given, understood* and *carried out.*

In order to test whether certain drugs other than those normally used would promote more rapid cure and enable the tissues to resist reinfection *without* surgical measures, 105 special cases were selected for experimental treatment and the general results tabulated.

Most of these cases had a history of persistent or recurrent infection (Table II).

TABLE II.

105 EXPERIMENTAL CASES.

	Total	No Improv.	Poss. Improv.	Improv.	Recurrence
MAPHARSIDE (ARSENOXIDE)	41	13	12	16	9
MAPHARSIDE WITH ZINC OXIDE & OIL OF CLOVES PASTE	3	3	–	–	–
NOVOSTAB (NEOARSPHENAMINE)	19	7	8	4	7
STABILARSAN (ARSPHENAMINE)	6	3	2	1	2
METAPHEN 1:500 (ORGANIC MERCURY COMPOUND)	13	5	5	3	3
PROPAMIDINE (M.&B. 782)	7	1	2	4	–
CIBAZOL OINTMENT (5% SULPHATHIAZOLE)	2	2	–	–	–
Zinc Peroxide 25% & Oil of Cloves Paste on wool	7	1	1	5	–
Zinc Oxide 3 parts, Pot.Chlor.1part &Oil of Cloves Paste on wool	11	–	2	9	1
ASCORBIC ACID DOSE 1200-2100 mg.	28	15	9	4	12
RIBENA (BLACKCURRANT SYRUP.) 20g. vit.C per fluid oz	19	9	8	2	8
NICOTINIC ACID DOSE 1050 - 2100 mg.	15	9	3	3	4
ESSOGEN (PURE VIT.A FREE FROM D.) DOSE 42000-252000 I.U.	20	8	6	6	9
TOTAL	191	76	58	57	55

It will be noticed from the total of 191 that many cases have been treated by more than one method, each therapy being used separately. In some instances several different methods were used successively and some individual case records are very interesting. The recurrences refer only to those cases which showed "Improvement" or "Possible improvement" and do not include those which showed "No improvement".

I tried to obtain a supply of penicillin for test purposes but was unable to do so. The three arsenical preparations were used locally only. Fusospirochætal organisms have not been demonstrated to penetrate the tissue affected and enter the general circulation in uncomplicated Vincent's lesions, and therefore in the present state of knowledge intravenous injections of arsenic would appear to be irrational. Reichmann (1926), Hirschfeld (1929), Daley (1931) and others all recommend the use of arsphenamine or neoarsphenamine locally, and Reichmann (1926) and Daley (1931) both state that intravenous injections are useless, while Goodridge (1942) and others have reported cases of Vincent's infection occurring during antisyphilitic treatment.

Previous experiments had shown that the arsenicals compared unfavourably with chromic acid and hydrogen peroxide therapy for the acute stage and these figures show that they were by no means specific in the later stages.

Mapharside was by far the most effective and promoted rapid healing in some stubborn cases. A sufficient number of successes were recorded for it to be included in the list of effective drugs to be used in intractable cases. It will be noticed, however, that without the subsequent removal of stagnation areas it did not confer immunity to reinfection.

Nine recurrences were observed out of the 28 cases which showed improvement. Seven recurrences out of 12 after novostab, and 2 out of 3 after stabilarsan were also recorded.

Packing with a mixture of zinc oxide and oil of cloves paste and a little mapharside has been suggested. Three cases were treated in this way and the results were all disastrous. Removal of the packs after twenty-four hours revealed exposed alveolar bone in each case. Fortunately the packs had not been left on long enough to cause necrosis of the bone, but great pain was experienced and healing was long delayed. Possibly the technique employed was faulty; nevertheless, I feel that this method should be strongly condemned.

Metaphen.—Thirteen cases were treated with metaphen which is an organic mercury compound in 1 : 500 solution. This preparation is used beneficially in streptococcal infections. Success was achieved in 3 cases and partial success in 5 others. Again there was no immunity to reinfection.

Propamidine.—Thrower and Valentine (1943), Kohn, Hall and Cross (1943), McIndoe and Tilley (1943), Morley and Bentley (1943), and Butler (1943) have reported success for this preparation in the treatment of chronic streptococcal infections, burns, ulcers and surgical infections; streptococci and other aerobes, and anaerobes including fusiform bacilli being effectively destroyed in a few days. They also noted that rapid re-epithelialization was promoted.

Propamidine 0·1% in a methyl cellulose mucilage was tried in 7 of these special cases but proved quite useless on gingival lesions because of the impossibility of sealing it in effectively. However, in 4 of the cases, infected sockets were present and these were packed with the propamidine jelly on cotton-wool. Rapid healing occurred in all 4 cases. Several more infected sockets have since been treated successfully, but difficulty has been experienced in retaining the dressings in position when the sockets have partly healed. In consequence, the technique has been adopted of dressing first with propamidine jelly until healthy granulations form and then filling the socket with B.I.P.P. This is left in position undisturbed until it is gradually extruded by progressive healing.

Cibazol.—Sulphathiazole powder mixed with zinc oxide and oil of cloves paste had previously been tried without success. It was thought that it might be retained in position round the teeth more easily in the form of an ointment, but trial proved that this was not so. Two cases were treated without improvement.

Packing with zinc oxide and oil of cloves paste on cotton-wool wisps has been proved to be a therapy of superlative merit. It was decided to try to establish if any further improvement over the routine method could be obtained by using zinc peroxide instead of zinc oxide. Mallett and Guralnick (1942) have used a watery paste of zinc peroxide with success in the treatment of mouth infections including Vincent's ulceration, its value being attributed to the slow and long-continued liberation of its oxygen. Unfortunately no greater concentration than a 25% zinc peroxide mixture with zinc oxide could be obtained and therefore a proper test could not be carried out. Packing with zinc peroxide—zinc oxide mixture and oil of cloves paste did prove to be beneficial, but later experiments comparing zinc peroxide mixture packs in one part of the mouth with control zinc oxide packs in another showed that the lesions healed equally well in both areas. A paste of zinc oxide 3 parts and pot. chlor. 1 part with oil of cloves was then tried with satisfactory results, but again control experiments showed that plain zinc oxide packs were equally beneficial.

Another series of vitamin tests was also undertaken, during which local treatment was confined to thorough cleansing and the application of one of the aniline dyes. The results in general were even less satisfactory than those recorded in the earlier series (Stammers 1944), and the number of recurrences was considerably greater than when local treatment of a more potent nature was employed.

With ascorbic acid, only 4 cases showed definite improvement and 9 possible improvement out of 28 and there were 12 recurrences.

The addition of Vitamin P had already been tried in a few cases without noticeable effect, but the possibility of some other vital factor being present in the natural source of supply which was absent in the synthetic product could not be ignored. Ribena black-currant syrup was therefore tried in 19 cases. It was obviously impossible to give sufficient syrup to equal the usual dosage of ascorbic acid and the total amount of vitamin C received was very small. Only 2 cases showed real improvement and 8 possible improvement and 8 had recurrent infection.

Three cases responded favourably to nicotinic acid, in 3 others there was partial improvement and 4 became reinfected.

In the earlier series a higher proportion of cases had responded favourably to the administration of small doses of essogen (pure vitamin A free from D) than to ascorbic acid or nicotinic acid. In these experiments it was decided to increase the dose for some patients. The previous total dose varied between 42,000 and 168,000 I.U. The response was fairly satisfactory (6 improvement and 6 possible improvement), but unfortunately only of limited duration and the number of recurrences in the absence of continued and complete local treatment was high.

From the examination of the collective results of treatment of these special cases (and previous experience with many other drugs gave similar results), it is apparent, therefore, that there is no easy and certain drug therapy which will cure persistent Vincent's lesions and confer immunity to reinfection. Experience has shown conclusively that, not only is early and thorough mechanical cleansing essential as a basis for the success of any therapy, but that such cleansing *must be continued progressively throughout treatment*. This progressive operative procedure begins with the careful removal of slough and tartar deposits from the ulcerated area at the first visit. All but a few patients tolerate this well and even the few can be treated with the aid of a surface anæsthetic paint. It must be emphasized that only the ulcerated area should be scaled before the acute infection is under control and re-epithelialization has started. This technique is not in accordance with accepted practice since many writers condemn too early scaling on the ground that it causes extension of the ulceration. No such harmful result has been noticed by us. In this connexion it is appropriate to record that on several occasions gingivectomy under nitrous oxide anæsthesia was performed at the height of acute infection in order to obtain biopsy material. Routine adoption of this practice is of course unwise, as there is a definite risk of infected material being aspirated into the lungs. Special care was taken to minimize this risk. As far as the local condition was concerned on no occasion was extension of ulceration observed; in fact, the total treatment time was considerably reduced in every case.

After mechanical cleansing the method of choice for the destruction of the bulk of the invading organisms is the use of 20% chromic acid and hydrogen peroxide. Usually two or three daily applications are sufficient; the use of this powerful escharotic for too long retards rather than accelerates cure by destroying the new epithelium. Unaffected parts of the mouth are thoroughly atomized and painted with a mild antiseptic at the same time.

Optimum results can only be obtained if efficient surgical treatment is supplemented by thorough home treatment by the patient. The use of toothbrush or sticks is contra-indicated during the acute stage lest possible trauma cause a spread of infection, and frequent mouth washing is the only safe method of cleansing. It has been found necessary to instruct nearly all patients in the correct muscular action needed to sluice the mouth-wash forcibly backwards and forwards between the teeth. The patient must also co-operate by securing free bowel action, particularly during the first few days of treatment when the elimination of toxic products is essential.

Immediately the acute infection is under control both surgery and home treatment are directed towards the restoration of a healthy gingival condition of the *whole mouth*. To this end the next step in the surgery is scaling of all the teeth, preceded and followed by a mild antiseptic paint. Any pockets or interdental stagnation areas now receive special attention and are best packed immediately with zinc oxide and oil of cloves paste on wool. It is also best to pack the original site of infection at this stage but the time factor has to be considered and this method, though desirable, is frequently impracticable. Again it is most important to stress the absolute necessity for treating the whole mouth by some method or other at each visit. Neglect of this essential has on many occasions resulted in either a persistent subacute infection or even an exacerbation at the original site, or else a fresh outbreak in some remote pocket or interdental space; in the latter instance reinfection of the original area will almost certainly follow unless adequate precautions are taken.

Next the extraction of roots and unsaveable teeth is carried out under antiseptic conditions. Where there is overcrowding of the teeth, with interdental spaces which cannot be rendered accessible, judicious extractions are preferable to the risk of recurrence. If it is clear by now that the prescribed home treatment is not being done in spite of repeated instruction and demonstration and that little or no enthusiasm can be aroused, the decision regarding extractions must be much more drastic, even to the extent of clearance of all teeth.

Finally, all parodontal pockets are eradicated. Sometimes this can be accomplished by packing alone, sometimes by electric cautery and packing, but in most cases only by

Nine recurrences were observed out of the 28 cases which showed improvement. Seven recurrences out of 12 after novostab, and 2 out of 3 after stabilarsan were also recorded.

Packing with a mixture of zinc oxide and oil of cloves paste and a little mapharside has been suggested. Three cases were treated in this way and the results were all disastrous. Removal of the packs after twenty-four hours revealed exposed alveolar bone in each case. Fortunately the packs had not been left on long enough to cause necrosis of the bone, but great pain was experienced and healing was long delayed. Possibly the technique employed was faulty: nevertheless, I feel that this method should be strongly condemned.

Metaphen.—Thirteen cases were treated with metaphen which is an organic mercury compound in 1 : 500 solution. This preparation is used beneficially in streptococcal infections. Success was achieved in 3 cases and partial success in 5 others. Again there was no immunity to reinfection.

Propamidine.—Thrower and Valentine (1943), McIndoe and Tilley (1943), Morley and Bentley (1943), Kohn, Hall and Cross (1943), and Butler (1943) have reported success for this preparation in the treatment of chronic streptococcal infections, burns, ulcers and surgical infections; streptococci and other aerobes, and anaerobes including fusiform bacilli being effectively destroyed in a few days. They also noted that rapid re-epithelialization was promoted.

Propamidine 0·1% in a methyl cellulose mucilage was tried in 7 of these special cases but proved quite useless on gingival lesions because of the impossibility of sealing it in effectively. However, in 4 of the cases, infected sockets were present and these were packed with the propamidine jelly on cotton-wool. Rapid healing occurred in all 4 cases. Several more infected sockets have since been treated successfully, but difficulty has been experienced in retaining the dressings in position when the sockets have partly healed. In consequence, the technique has been adopted of dressing first with propamidine jelly until healthy granulations form and then filling the socket with B.I.P.P. This is left in position undisturbed until it is gradually extruded by progressive healing.

Cibazol.—Sulphathiazole powder mixed with zinc oxide and oil of cloves paste had previously been tried without success. It was thought that it might be retained in position round the teeth more easily in the form of an ointment, but trial proved that this was not so. Two cases were treated without improvement.

Packing with zinc oxide and oil of cloves paste on cotton-wool wisps has been proved to be a therapy of superlative merit. It was decided to try to establish if any further improvement over the routine method could be obtained by using zinc peroxide instead of zinc oxide. Mallett and Guralnick (1942) have used a watery paste of zinc peroxide with success in the treatment of mouth infections including Vincent's ulceration, its value being attributed to the slow and long-continued liberation of its oxygen. Unfortunately no greater concentration than a 25% zinc peroxide mixture with zinc oxide could be obtained and therefore a proper test could not be carried out. Packing with zinc peroxide—zinc oxide mixture and oil of cloves paste did prove to be beneficial, but later experiments comparing zinc peroxide mixture packs in one part of the mouth with control zinc oxide packs in another showed that the lesions healed equally well in both areas. A paste of zinc oxide 3 parts and pot. chlor. 1 part with oil of cloves was then tried with satisfactory results, but again control experiments showed that plain zinc oxide packs were equally beneficial.

Another series of vitamin tests was also undertaken, during which local treatment was confined to thorough cleansing and the application of one of the aniline dyes. The results in general were even less satisfactory than those recorded in the earlier series (Stammers 1944), and the number of recurrences was considerably greater than when local treatment of a more potent nature was employed.

With ascorbic acid, only 4 cases showed definite improvement and 9 possible improvement out of 28 and there were 12 recurrences.

The addition of Vitamin P had already been tried in a few cases without noticeable effect, but the possibility of some other vital factor being present in the natural source of supply which was absent in the synthetic product could not be ignored. Ribena black-currant syrup was therefore tried in 19 cases. It was obviously impossible to give sufficient syrup to equal the usual dosage of ascorbic acid and the total amount of vitamin C received was very small. Only 2 cases showed real improvement and 8 possible improvement and 8 had recurrent infection.

Three cases responded favourably to nicotinic acid, in 3 others there was partial improvement and 4 became reinfected.

organisms in the tissues that are not accompanied by active tissue reaction, or that do not show the accepted distinctive morphological picture". He is of the opinion that "there is probably a phase in the life cycle of many common organisms during which atypical morphology and absence of tissue reaction are cardinal features. Presumably such phases pass and the organisms resume normal growth with altered immunity reactions of the host". And he states that "such demonstration of chronic sepsis in the sphenoid bone has not been previously made, and it may help to explain why clinically many cases of sinus disease do better when the highly reactive membrane of the affected sinus is removed completely".

Little is known of the life-history of Vincent's organisms although R. and M. Dean (1931), Tunnicliff (1939) and others claim to have demonstrated a life-cycle in which the fusiform bacillus and the spirochæte are different morphological forms of a higher bacterium or microscopic plant. If their views are accepted it is conceivable in the light of Pickworth's findings that atypical morphological forms, possibly gonidia, of viable organisms may remain in the gingival tissue enclosing the pockets even after clinical cure of the disease, and after variable periods of dormancy may resume normal growth and re-establish clinical ulceration.

The third possible explanation of the phenomenon of recurrent infection of the same area, is that of localized sensitivity of the tissue cells to the fusospirochætal organisms. Allergic sensitivity of cells to some bacteria has been proved experimentally by growth *in vitro* (tissue culture) (Aronson, 1931; Moen, 1937). The assumption that cells of the subgingival tissue do become sensitized to Vincent's organisms means that the reappearance of these organisms in the pocket would provoke a reaction in the adjacent soft tissues to combat the toxic effect upon the sensitized cells. Part of this reaction would take the form of a hyperæmia in order to provide increased oxygenation of the threatened area; but hyperæmia of the gum papilla, exposed as it is to intermittent traumatic injury, always results in rupture of some of the capillaries with hæmorrhage, thrombosis and congestion. Thus the allergic reaction would soon defeat its own object and result in a condition of ischæmia, providing in a comparatively short time conditions actually favouring the proliferation of the fusospirochætal flora and the recurrence of ulceration.

Sections of several specimens of gingival tissue taken from acute, subacute and healed lesions have been prepared, and examined microscopically. Numbers of fusiform bacilli and spirochætes have been constantly seen in necrotic areas, and also superficial invasion of the *living* tissue in sections from clinically infected cases, but no recognizable forms have been seen in sections from healed lesions.

Photomicrographs of a section of gum (stained in bulk with silver) taken from an acute case show large numbers of fusospirochætal organisms in the slough and attacking the remaining subgingival epithelium, but no deep penetration of the tissues by the organisms can be demonstrated.

In many specimens of gingival tissue taken from healed Vincent's lesions which appeared, clinically, to be on the point of breaking down again, vascularization of the epithelium has been observed. The photomicrographs show projections of the connective tissue papillæ, in many cases consisting solely of blood-vessels, extending nearly to the surface of the epithelium and frequently turning and lying parallel to it, particularly in the epithelium lining the pocket. Many sections through the series have to be examined before the connexion of these transversely cut papillæ with the gum corium can be traced. The ease with which slight pressure on the gum causes hæmorrhage from the pocket can be readily understood when it is seen how near to the surface the blood-vessels approach, and how prone are the tissues to attack by organisms situated in the pocket if the vessels become congested and stasis ensues. The high magnification of one papilla shows several vessels packed with red cells, and œdema and disintegration of the overlying epithelial cells. (The photomicrographs cannot be reproduced owing to lack of space.)

It seems obvious that vascularization of the epithelium is part of a defence mechanism, and if any particular significance can be attached to its association with healed Vincent's lesions on the verge of recurrence, it does suggest that there may be a connexion between this phenomenon and local tissue sensitivity, which may be, therefore, a probable explanation of reinfection. A great deal of careful research is still needed before a correct answer can be given and therefore, in the present state of our knowledge, these explanations of recurrent infection must remain hypothetical.

(The histories and progress of treatment of five cases were then given and illustrated by lantern slides of photographs in colour, smears, and photomicrographs.)

the radical operation of gingivectomy, the whole mouth receiving attention at the same time. In many instances deterioration has been observed in one part of the mouth while another part is being treated by gingivectomy, and usually it is advisable to keep all pockets packed pending their elimination. Subgingival calculus which was previously inaccessible is now removed, the teeth carefully polished and any cavities restored.

That gingivectomy is almost always successful in the prevention of recurrence has been proved by experience, and during the last twelve months only three cases of reinfection of the area so treated have been observed; in each there had been complete neglect of oral hygiene. Many cases have been seen in which ulceration has subsequently occurred in previously unaffected areas, such as around erupting wisdom teeth, and the area previously infected and treated by gingivectomy has remained perfectly healthy.

In addition to these surgical and other operative measures, which after all are only a means to an end, there is a much more important and difficult task: that of educating the patient in the maintenance of oral health. As soon as healing of the ulcers is well established additional home treatment consists of thorough cleaning and massage of all accessible parts of the mouth with a toothbrush and a mixture of equal parts of salt and bicarbonate of soda for several minutes after each meal and at bedtime. The softest grade of brush obtainable should be used at first and a medium grade later. Unfortunately several cases of brush trauma have been observed recently owing to the difficulty of getting a soft brush at the present time. I do not think it is wise to use wooden sticks between the teeth until the pockets have been removed, and anyway there are probably zinc oxide packs in position, but as soon as the pockets have been eliminated and the packs removed Fish's friction technique with wooden sticks is started. Keene's soft wood sticks are used at first, and later, when the epithelium is well keratinized, sharpened match-sticks. Without this technique there is always the tendency for tissue to grow up interdentally with the inevitable formation of new pockets and the return of ulceration.

Now I propose to turn very briefly from the results and details of treatment to the consideration of a possible explanation of the proved success of gingivectomy. Parodontal pockets have been shown to be present in practically 100% of mouths infected by Vincent's organisms, yet it is an undoubted fact that those pockets and small numbers of those same organisms have been present for a long time before the initial attack. It is also a fact, that, in many cases if the pockets are left, destruction of the bulk of the bacterial flora and elimination of the contributory factors as far as possible may still be followed in a comparatively short time by reinfection of the same area, while removal of the tissue enclosing the pockets by cautery or excision confers immunity for a long period, even when the contributory factors remain unchecked and previously virulent organisms are present in other parts of the mouth.

Does the explanation of this phenomenon depend upon the mere presence of the pockets or is it concerned with the tissues enclosing the pockets? In other words, do the surviving organisms (originally saprophytic and having slowly acquired maximum pathogenicity during months or even years in a favourable habitat) maintain their virulence in the pockets and again cause ulceration, and does the obliteration of the pockets simply deny them a suitable nidus; or does the gingival tissue remain infected by organisms which lie dormant in the tissue for a time and later resume normal growth; or does the tissue itself acquire some quality which renders its reinfection inevitable in the course of time?

The first possibility would account for the repeated slight exacerbations seen in persistent cases when treatment has been interrupted for a day or two or when the whole of the mouth has not been treated at each visit, but it does not appear to offer a complete explanation of periodic flare-ups occurring after a month or two of apparent health; neither does it explain why the same area becomes the site of ulceration time after time. These sequelæ would, however, be accounted for if either the second or third possibility could be shown to be true.

The work of Pickworth on the Histobacteriology of Chronic Nasal Sinusitis (1943) may have a bearing upon the second possibility (i.e. organisms remaining dormant in the tissues). He has examined large numbers of pathological sinus membranes and specimens of sphenoid bone adjacent to the sinus, and while generally the tissues were found to be sterile, in some cases he has demonstrated pleomorphic forms of streptococci growing in the living, but ischæmic, tissue unaccompanied by active tissue reaction. He considers that, "because of the scarcity and pleomorphism of the organisms when grown under adverse conditions, pathologists, who deal generally with a superabundance of perfectly shaped organisms produced in ideal cultural surroundings, may tend to overlook a few

Section for the Study of Disease in Children

President—ERIC A. CROOK, M.Ch.

[*March* 24, 1944]

HELD AT THE HOSPITAL FOR SICK CHILDREN,
GREAT ORMOND STREET, LONDON, W.C.1

Acute Sinusitis and Technique of the Antrum Washout.—JAMES CROOKS, F.R.C.S.

Mr. James Crooks showed five children suffering from nasal accessory sinusitis, and illustrating complications which may arise from such disease.

He emphasized the frequency of such infections and demonstrated the technique of antrum lavage under local anæsthesia in the young subject.

In answer to questions he stated that sinus infection in the child was usually curable by non-operative measures, and that the early recognition of the condition was essential to the prevention of advanced disease requiring operation.

Tuberculosis of Right Hip, with Chronic Miliary Infection of Lungs.—WILFRED SHELDON, M.D. (shown by B. J. HUSSEY, M.R.C.S., L.R.C.P.).

C. C., aged 7 years.

History.—Onset of pain in right leg in November 1943, following a fall from a lorry. Seen in out-patient department, and found to have limitation of all movements of right hip-joint, with pain. No wasting.

Past history.—Nothing relevant. No history of contact with tuberculosis. Parents alive and well.

November 1943: Admitted to hospital for investigation. Right hip showed limitation of abduction, internal rotation, and external rotation, with slight limitation of flexion. Mantoux 1:1,000 was strongly positive.

Blood sedimentation rate: 42 mm. in one hour.

X-ray of chest showed typical miliary tuberculosis.

On admission to Tadworth Court (January 1944).—General condition was quite good, but appetite very poor.

Lungs: On clinical examination fine râles were present at the right base, with slight diminution of air-entry in this area.

X-ray: Miliary tuberculosis. No change from appearance two months ago. No evidence of tuberculous meningitis.

Optic discs: No tubercles. Urine: Nothing abnormal.

Blood sedimentation rate: 61 mm. in one hour. Gastric lavage: No tubercle bacilli.

March 1944: General condition has definitely improved since admission. Is now eating well, and is looking very fit. Temperature remains normal.

X-ray chest: No change. X-ray hip: No improvement as yet, after three months in a plaster spica.

Constrictive Pericarditis: Pericardial Resection.—R. S. PILCHER, M.S. (shown by JANET D. GIMSON, M.B.).

Mavis P., aged 9, was admitted to Great Ormond Street Hospital for Sick Children in September 1943 with ascites which had been tapped at weekly intervals for nearly a year. Her illness appears to have started with an acute pericarditis in June 1942. Besides ascites she had had bilateral pleural effusions and had much œdema of the legs.

REFERENCES

ARONSON, J. D. (1931) *J. exp. Med.*, **54**, 387.
BUTLER, E. C. B. (1943) *Lancet* (ii), 73.
DALEY, E. H. (1931) *J. Amer. dent. Ass.*, **18**, 495.
DEAN, R. D., and DEAN, M. T. (1931) *J. dent. Res.*, **11**, 759.
GOODRIDGE, D. L. (1942) *Brit. dent. J.*, **72**, 12.
HIRSCHFELD, I. (1929) *J. Amer. dent. Ass.*, **16**, 623.
KOHN, F., HALL, M. H., and CROSS, C. D. (1943) *Lancet* (i), 140.
MALLETT, S. P., and GURALNICK, W. C. (1942) *J. Amer. dent. Ass.*, **29**, 384.
McINDOE, A. H., and TILLEY, A. R. (1943) *Lancet* (i), 136.
MOEN, J. K. (1937) *J. exp. Med.*, **65**, 587.
MORLEY, G. H., and BENTLEY, J. P. (1943) *Lancet* (i), 138.
PICKWORTH, F. A. (1943) *J. Laryng.*, **58**, 188.
REICHMANN, F. J. (1926) *J. Amer. dent. Ass.*, **13**, 1665.
STAMMERS, A. F. (1944) *Brit. dent. J.*, **76**, 147, 171, 205.
THROWER, W. R., and VALENTINE, F. C. O. (1943) *Lancet* (i), 133.
TUNNICLIFF, R. (1939) *J. Amer. dent. Ass.*, **26**, 1987.

Mr. Arthur Bulleid: I have always felt that Vincent's infection has become far too much a *bête noire* to the dental surgeon. Perhaps this is partly due to the fact that so many patients suffering from this disease go to their doctors first and not their dental surgeons and this often results in valuable time being lost before adequate dental treatment is commenced.

I am extremely pleased that Mr. Stammers has stressed the importance of the "stagnation" picture in the incidence of the disease and possible reinfection and recurrence. To a large extent this is the clue to the question of recurrence and reinfection and if we can get rid of stagnation areas by our own treatment and then imbue the patient with the necessity of close co-operation with a view to preventing further stagnation; we shall be well on the way to success.

The weight of evidence is against those who think the disease is infectious, but I am not so certain about the question of contagion, and I think precautions should be taken against contagion. Mr. Stammers will undoubtedly agree that cases of recurrent infection or persistent infection will be greatly minimized if the original acute lesion is treated adequately at its inception, both by the dental surgeon and the patient. It is surely when one or both fail in their treatment of the acute case that subsequent trouble occurs.

In the present state of our knowledge we simply do not know what is the causal organism of Vincent's infection. It has been so long the custom to consider that the fusiform bacillus and its accompanying *T. vincenti* are the causal organisms that one is apt to forget that there is as yet no proof that they are, in fact, causal. It has been impossible to produce Vincent's infection experimentally in animals and apparently there is no humoral immunity conferred by them. All that at present can be claimed is that these organisms are of diagnostic significance.

I would also stress another point—in a "clean" mouth the fusiform bacilli and spiral forms are almost conspicuous by their absence. Undoubtedly stagnation favours their appearance and growth. I think this point shows clearly how useful the routine "gum smear" examination can be.

Mr. Stammers has found no place for trichloracetic acid in the treatment, but I have found this drug exceedingly useful in acute cases and I always cauterize the ulcers with a 50% solution before I pack with the zinc oxide—oil of cloves paste. It eases pain almost at once, and pain is a marked feature of the acute ulceration.

I generally leave my "packs" in place for four days before removal. Because I use trichloracetic acid I have not found it necessary to worry about the debris around the teeth, and scaling, &c., can be safely left till the packs are removed. I should not, however, hesitate to remove sloughs in the acute phase of the disease if I thought it the better way.

I agree that vitamin therapy by itself has been most disappointing. As an adjunct to local treatment some cases are helped, but I have not found that it has accelerated the rate of cure or prevented recurrences.

With reference to the question of treatment after the "pockets" have been eradicated I am a firm believer in the efficiency of gum massage with an aqueous solution of tannic acid, and I always show the patient how to carry out the massage.

To my mind recurrence is undoubtedly due to failure to eliminate stagnation areas, sometimes inadvertently but often from a failure to appreciate their importance. I have found that if adequate treatment is instituted quickly in the acute stage then in quite a number of cases gum massage and toothpick drill make gingivectomy unnecessary though loose interdental papillæ may have to be excised.

Stagnation is also a possible explanation of the great increase in the fusospirochætal flora in cases of Vincent's disease. In the pockets the pH is alkaline and this favours their growth. Remove the pocket and the pabulum favourable to the fusospirochætal flora is taken away.

In the present state of our knowledge it is impossible to say if the possible localized sensitivity of the tissue cells to the fusospirochætal flora is a factor or not as we do not know what is the significance of these organisms, or what part they play in the disease.

saccular or fusiform bronchiectasis 5 patients are absolutely well, freedom from symptoms is commonest in unilateral tubular cases. The shape of the bronchi and the number involved remain remarkably constant. Rarely the lesion may resolve and 2 such cases have been observed. In 1 case tubular has progressed to saccular dilatation and in 1 the disease seems to have spread to the other lung during observation. Chronic upper respiratory infections, meaning actual pus in sinuses or chronic middle-ear disease, contribute to the continuance of symptoms and if such infection can be cleared up, by so much is the outlook improved. Clubbing of the fingers was a disappointing sign, being present in only 5 cases. It had been present in 3 other cases, all clinically improving, 2 now having normal fingers, and 1 curved nails. Growth was impossible to assess in the absence of standard height and weight tables.

Pulmonary collapse was clearly present in 10 out of 24 cases, and is permanently present in 6. It seems to be a common accompaniment of unilobar tubular bronchiectasis and seems not to affect the satisfactory prognosis of these cases.

As in so many chronic diseases, the case may have a prolonged and serious onset, becoming at once and remaining of classical type, with characteristic physical and X-ray signs and purulent sputum. Usually the extent of the disease is determined at the onset. Some such cases, especially in the absence of foul sputum, may improve after months or years, and this result is more likely if any upper respiratory infection present can be cleared up, and if fresh pulmonary infection can be avoided by improving living conditions from the point of view of crowding, dampness, fresh air and suitable schooling. There is undoubtedly a large group where the initial illness is short-lived and where the *diagnosis depends on medical curiosity. These cases would not have been diagnosed* before the days of bronchograms and include many with unilobar tubular bronchiectasis of which the prognosis during childhood is good.

It is hoped that the series will remain under observation and perhaps will be reported on again in twenty-five years' time.

TABLE I.

Case*	Probable duration of disease in years	Observation period in years	Onset from
Invalid :			
3	16	10	Measles and pneumonia at 4 years : died at 20 years
4	15¾	9	Birth : pink disease 9 months
6	14	12	Diphtheria at 4 years
7	13¾	7½	Pneumonia at 3 months
11	12¼	10	Whooping-cough and pneumonia at 2 years
Delicate :			
8	13½	4	Pneumonia at 1 year
12	12½	5	Birth
19	9	9½	Diphtheria at 4 years
21	8¼	7¼	Measles and pneumonia at 2½ years
Absolutely well :			
1	21	9½	Whooping-cough at 3 weeks
2	18½	9	Pneumonia at 8 months
5	15	5½	6 months insidiously
9	13	6½	Pneumonia at 4 years
10	13	10	Birth
13	12½	10	Pneumonia at 4 years after T. and A.
14	12	8¾	Pneumonia at 1¾ years
15	11	9¼	Diphtheria at 6¼ years
16	10½	5¼	2 years insidiously
17	10¼	6¼	Whooping-cough at 8 years
18	10	7¼	2 years insidiously
20	8¼	5¼	Measles at 4 years
22	7	6	4 years insidiously
23	5¼	4¼	Whooping-cough at 4½ years
24	4½	4	Pneumonia at 3½ years, complicating burns

* Cases numbered according to probable duration of disease.

TABLE II.

Class	Total	Shape of dilatation			Lung involvement		Nails			Sinuses			
		Tubular	Fusiform	Saccular	Unilateral	Bilateral	Clubbing	Curved nails	Normal	Pus	X-ray positive	Normal	Not examined
Invalid	5 (1 dead)	0				4	2	3	0	1	2	1	1
Delicate	4	1				3	2	2	0	2	2	0	0
Absolutely well	15	10				14	1	1	4	10	0	4	6	5

On admission she had orthopnœa, moderate cyanosis of the face and hands and intense cyanosis of the feet. Signs of constrictive pericarditis were: distended cervical veins showing no inspiratory collapse, low blood-pressure with no measurable pulse-pressure, a small, still quiet heart, serous effusions and œdema of the legs. X-ray confirmed diminished movement of heart.

Pericardial resection was performed in October 1943 but although the heart was well released there was no improvement at first in the pulse pressure. Cyanosis and venous engorgement were less but fluid continued to accumulate in the belly.

A month after operation when she was sufficiently improved to be about on her feet a little, she suddenly had a series of convulsions lasting three hours. No explanation of these was found but during them for the first time the systolic pressure rose to over 100 and both systolic and diastolic readings were obtained for the first time by auscultation. During the fits she was intensely cyanosed and the intervals were so short that her colour was never restored by oxygen until the fits ended. It was feared that she might have suffered some permanent cortical damage and her mental condition gave rise to anxiety for several days. However, she appeared to make a complete mental recovery and began to get about again. Her pulse-pressure remained normal but there was still repeated re-accumulation of ascites.

In January this year she was transferred to a convalescent hospital and almost immediately her belly began to shrink and no further tapping was required.

Intrathoracic Cyst of Gastric Type: One-Stage Removal.—R. S. PILCHER, M.S. (shown by C. ELAINE FIELD, M.D.).

Margaret B., aged 1 year, was admitted to Hemel Hempstead Hospital in September 1941 with a history of swelling of the belly and unsatisfactory progress for five months.

It was obvious on examination that the child had a large space-occupying lesion in the right side of the chest and there was considerable speculation as to its nature, especially as to whether it was benign or malignant. Unfortunately the possibility of its being an intestinal cyst was not considered and therefore no examination of the aspirated contents was made for enzyme activity. The swelling of the belly appeared to be due to downward displacement of the liver.

The cyst was removed on 16.10.41. The operation did not offer any great difficulty and was well borne by the child. The cyst appeared to have its main attachment and blood supply in the upper part of the paravertebral gutter, where no doubt the sympathetic was damaged since the child after operation had Horner's syndrome and a dry upper eyelid.

Of interest is the rapid re-expansion of the lung which presumably had been collapsed for some months.

[April 28, 1944]

The Prognosis of Bronchiectasis in Childhood [Abstract]

By A. WHITE FRANKLIN, F.R.C.P.

THE prognosis is reviewed in 24 cases of bronchiectasis in children observed clinically and radiologically for periods ranging between four and twelve years. Once bronchiectasis is recognized, that is, where there is definite bronchial dilatation shown by a bronchogram, what will happen to the child's health, growth, and chances of survival? Does dilatation spread to involve new bronchi, new lobes or the other lung? Does the shape of the dilatation matter and does it alter? Does spontaneous recovery occur?

The cases have been classed as (1) those "absolutely well", able to live normal lives free from symptoms, (2) those "delicate", i.e. well for the most part but requiring special care, extra rest, convalescent home or residential school and liable to periodic, mild, short-lived febrile attacks with cough and perhaps sputum, and (3) "invalids" who by reason of poor general condition or constant cough with sputum are prevented from living a normal life. Of the 24 cases 15 are absolutely well, of whom 6 have been earlier in the delicate or invalid class, 4 are delicate, and 5 are in the invalid class, one of whom has died. In Table I the cases are numbered in the order of probable duration of the disease. Table II shows the three classes broken up according to the shape of the dilatation, to number of lungs involved, to the presence of clubbing and of sinus infection.

The study of these cases suggests the following conclusions: The age and type of onset and the duration of the disease do not directly affect the prognosis. Though of 13 with

operation, but with increasing experience we have a better understanding of the hazards of operation and how to deal with them. Although there have been 7 deaths in the whole series of 60 operations there has been none in the last 30 (*see* Table II). Reduction in mortality may be due in small part to experience of operative technique but is

TABLE II.—MORTALITY AND MORBIDITY OF SURGICAL TREATMENT OF BRONCHIECTASIS

Mortality	
Died at operation	4
Died within twenty-four hours of operation ...	3
Died after twenty-four hours	0 —
	7
Details of seven fatal cases	
Pneumonectomy	2
Second lobectomy in bilateral case	1
First lobectomy in bilateral case	1
Double lobectomy in unilateral case	1
Single lobectomy in unilateral case	2 —
	7
Morbidity	
Empyema	10
Pleural infection, not purulent	1
Bronchiectasis in residual lobe	3
Bronchial fistula	3
Wound infection without empyema	1 —
	18
Details of empyema	
After pneumonectomy	2
With burst bronchus 1	
Without burst bronchus 1	
After left lower and lingular lobectomy	7
After left lower lobectomy	1 —
	10
Results in empyema cases	
Healed	6
With fistula 2	
Not yet healed	4
With fistula 1	—
	10

mainly attributed to more thorough preoperative preparation and to control of bronchial secretion at operation. The preoperative preparation is essentially the medical treatment of the disease and we prefer not to operate until we think the patient has the maximum benefit therefrom. At operation we rely for control of bronchial secretion mainly on bronchoscopy immediately before and after operation but we also use aspiration through the intratracheal anæsthetic tube.

There are two complications which we have not yet learnt how to prevent, empyema and delayed re-expansion of residual lobes. Of these the latter is the more important and in the absence of atelectasis empyema is much less serious. No doubt many pleural infections occur at the time of operation but we have seen them develop late in cases where there has been persistent atelectasis. The most serious aspect of atelectasis, however, is not its association with empyema but the occasional development of bronchiectasis in the residual lobes, and in three cases we have had to remove a previously healthy upper lobe for this indication. In two of these there was empyema and atelectasis of the upper lobe after resection of left lower lobe and lingula. In the third, after left lower lobectomy the upper lobe re-expanded but collapsed again after the child had left hospital, and when she was seen again the upper lobe bronchus was found partly blocked by a granuloma arising from the lower lobe stump. Of the possible causes of post-operative atelectasis obstruction of the bronchus is almost certainly the most important. For this reason patients are encouraged to expectorate after operation as soon as they are conscious and if re-expansion is delayed bronchoscopic aspiration is done. In the prophylaxis of empyema chemotherapy *may* be of value but so far we have found no evidence of this in a parallel series of controls and cases treated by local application of sulphonamides in the pleura. Empyema has in our experience been particularly associated with resection of the left lower lobe and lingula and this may be due to leakage from the cut surface of the upper lobe made in separating the lingula. If so, we may expect the same difficulty with segmental resections. We do not drain the pleura as a routine but sometimes put in a fine intercostal tube which is kept closed except for daily aspiration. This has no advantage over aspiration with a needle except that it requires less fortitude on the part of the patient and children do not take kindly to repeated needling. In the treatment of empyema we have recently had some success with penicillin but this does not justify an attitude of complacence towards this complication. Moreover penicillin cannot be expected to cure an empyema if there is a large bronchial fistula, although a small one is no contra-indication to its use.

Surgical Treatment of Bronchiectasis in Children

By R. S. Pilcher, M.S.

RESECTION of lung for bronchiectasis is done on the assumption that there is an irreversible change in the lung which condemns the patient to chronic ill-health if not an early death, and that its removal holds out a hope of complete and permanent cure. How far this hope is justified remains to be seen, and although some of the earlier cases have grown into robust adolescents, many years must pass before we know how they will fare in adult life. Our aim has been to remove all the diseased lung and, no case has been rejected for surgery in which this was thought possible (*see* Table I). We

TABLE I.—SURGICAL TREATMENT OF BRONCHIECTASIS IN CHILDREN IN THE SURGICAL UNIT, UNIVERSITY COLLEGE HOSPITAL

Cases completed			35
Cases still under treatment—			
Bilateral, awaiting second operation ...			8
Unhealed empyema, resection completed			4
		Total cases ...	47

Extent of disease in 47 cases					
Unilateral	3 lobes				7 cases
	2 lobes				5 cases
	1 lobe				15 cases — 27
Bilateral	3 and 1 lobes				2 cases
	2 and 2 lobes				2 cases
	2 and 1 lobes				11 cases
	1 and 1 lobes				5 cases — 20

Extent of resection in 39 cases					
Unilateral	3 lobes				9 cases
	2 lobes				5 cases
	1 lobe				15 cases — 29
Bilateral	3 and 1 lobes				2 cases
	2 and 2 lobes				1 case
	2 and 1 lobes				6 cases
	1 and 1 lobes				1 case — 10

Extent of resection in 60 operations					
Pneumonectomy					8 cases
More than 1 lobe...					16 cases
1 lobe					36 cases — 60

do not yet know how much lung can be removed but unless all the part in which there is an irreversible change is excised there is no hope of cure, although incomplete surgical treatment may give such relief of symptoms as to make it worth while in some cases. The disease is not merely a septic process but, in addition the part of the lung which is collapsed or fibrosed acts as an arteriovenous shunt since the blood flowing through it in the pulmonary circulation is not oxygenated. This factor becomes important when there is sudden collapse of large areas, a common incident in bronchiectasis that may be mistaken for pneumonia. While it is essential for cure to remove all diseased tissue it is equally important, especially in extensive cases, to spare all that is healthy. For this reason the conception of the lobe as the minimal unit for resection should be abandoned. Churchill and Belsey (1939) have described segmental resection of the lung and reported its application to the lower lobe with preservation of the dorsal segment. We have recently completed a bilateral case in which only the lingula was removed on the left, and on the right the middle lobe and all of the lower except the dorsal segment. The amount of lung that can be removed depends on what happens to the residue, and about this we know little as yet but we believe that in children there is a possibility of true hypertrophy of the residual lung and that the danger of pathological emphysema is less than in adults. We have, however, already observed that in some children after extensive resections physical development seems to be retarded.

When we started this work we decided to use the method of dissection both for pneumonectomy and lobectomy (Pilcher and Byrde, 1941). By this method removal of the disease is more complete, bronchial closure and hæmostasis are more certain and bronchial stumps are of minimum length, we thought too, that there was less risk of pleural infection than with the tourniquet method. Our early mortality was discouraging and may have been due in part to the longer time required for the dissection

Anatomy: Bronchioles are of a size less than 1 mm. in diameter. The structure of the wall and the relationship to neighbouring lung tissue are, however, more characteristic than mere size.   In fact the bronchioles of about 1 mm. in diameter are really in structure intermediate between the bronchi and bronchioles and have been called by Engel bronchioli.

In contradistinction to the bronchi, which have thick walls permeated by fibrous tissue and reinforced by cartilage, the bronchioles are thin-walled, contain no cartilage, and have hardly any goblet cells, which are, of course, very numerous in the bronchi. The bronchioles are kept patent partly by the tone of the muscles and partly by the respiratory movements.   The bronchi are situated in the fibrous septa of the lung and are therefore, strictly speaking, extrapulmonary; the bronchioles, on the other hand, are situated directly in the lung tissue.   Bronchiolitis, therefore, is an intrapulmonary lesion and is in consequence more serious.

The bronchiole consists of the following layers from within outwards: (1) Epithelium, which is columnar and ciliated; (2) the elastic layer, made of closely-spaced elastic fibrils running longitudinally; (3) the basal membrane; (4) basal cells.   These are flat spindle-shaped cells, irregularly scattered and situated between the epithelium and the basal membrane; (5) muscular layer; (6) adventitia, consisting of connective tissue, elastic fibres and vessels.

1 —Columnar epithelium.
2 —Flat basal cells.
3 —Basal membrane.
4 —Elastic sheath.
5 —Muscles.
6 —Adventitia composed of connective tissue, elastic fibres and vessels.
7 —Alveolar walls.
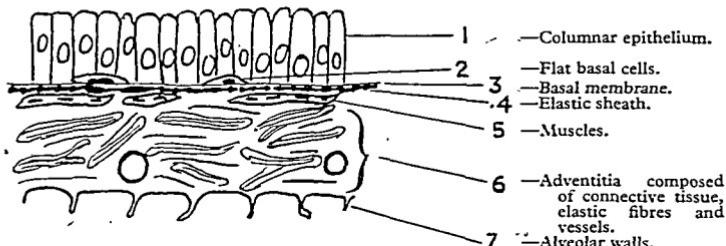
FIG. 1

Bronchiole 0·3 mm. ×·80. (From Engel and Newns, *Arch. Dis. Child.*, 1940, **15**, 225.)

PATHOLOGY OF BRONCHIOLITIS

(1) *Catarrhal.*—The mucous membrane alone is involved, the wall remaining unaffected. The epithelium is engorged and infiltrated with inflammatory cells, and there may be desquamation of the epithelial cells.
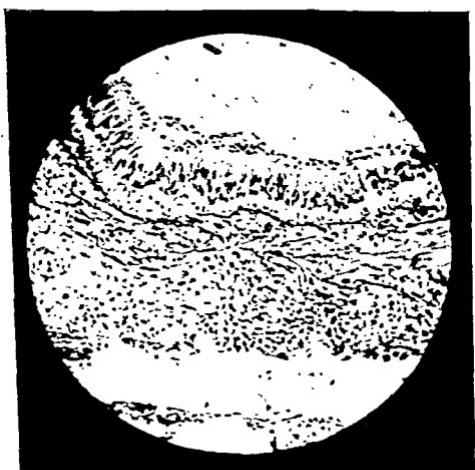
FIG. 2.—A high-power view (× 125) of a bronchiole showing the minute structure. *Cf.* diagram (fig. 1). The elastic layer is well seen. From a child aged 6 years.
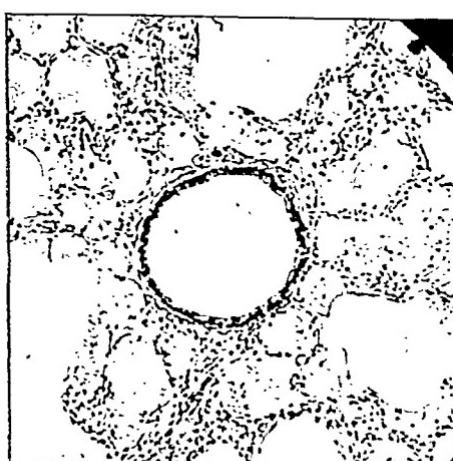
FIG. 3.—A bronchiole, *diameter 0·2 mm. in a child aged 3 months.* × 31.

With regard to results, Table III shows the present state of the completed cases. Recent cases in Class C are not to be regarded as failures since symptoms of bronchiectasis often persist for some months after operation, being due, we think, to associated bronchitis in the rest of the bronchial tree. The cases in Class B are of particular interest

TABLE III.—RESULTS OF OPERATION IN 28 COMPLETED CASES OF BRONCHIECTASIS.

Classification.
A. Free of symptoms and fit.
B. Free of symptoms but not fully fit.
C. Residual symptoms of bronchiectasis, improved.
D. No improvement or worse.

Interval			A	B	C	D	Total
3 to 5 years	...	...	4	1	1	—	6
2 years	...	...	2	1	—	—	3
1 year	...	...	5	1	2	—	8
Less than 1 year	...		8	1	2	—	11
Totals			19	4	5	—	28

because they seem to be cured of bronchiectasis but physical development is retarded and exercise tolerance below normal. We shall be interested to see if these children pick up later or remain handicapped by loss of lung tissue.

The complete treatment of bronchiectasis requires the best teamwork. Surgery is only an incident in this treatment and other measures are indispensable. Without collaboration from other members of the team at Great Ormond Street and University College Hospitals the Surgical Unit which I represent could not have done the work I have outlined here.

REFERENCES

CHURCHILL, E. D., and BELSEY, R. (1939) *Ann. Surg.*, **109**, 481.
PILCHER, R. S., and BYRDE, E. (1941) *Lancet* (i), 303.

Bronchiolitis in Children

By G. H. NEWNS, M.D.

ACUTE bronchiolitis was not until recently described under that name. It was usually called capillary bronchitis, a term which is still in use. Another name was acute suffocative catarrh because of the obstructive dyspnœa which is so characteristic a symptom. MacCallum and Opie, in the last war, called the disease interstitial bronchopneumonia, a name which is somewhat misleading.

A considerable difference of opinion exists as to the frequency of this condition: some even doubt its existence as a distinct entity, claiming that it cannot be distinguished either clinically or pathologically from bronchopneumonia.

The impression gained from the older pædiatric writings of some forty to fifty years ago is that acute bronchiolitis was then a much more common disease than it is to-day. This diminution in incidence may, of course, be largely due to the great improvement in the general health, environmental conditions, and medical care of the young infant of the present day.

Acute bronchiolitis, to-day, is not a common disease, at least as a sporadic complaint, though opinions on this point vary. There is no doubt, however, that its incidence rises sharply in epidemics of influenza, which is the commonest cause of acute bronchiolitis. Indeed Horder (Price's Medicine, 1933) states that "Capillary bronchitis is the essential lesion in influenza". Many cases were described in the pandemic of influenza at the close of the last war, and MacCallum (1919) described a remarkable series of cases in epidemics of measles occurring in U.S. Army camps during the war.

Acute bronchiolitis may occur in pertussis as well as in influenza and measles, and occasionally in other infections though in these latter the pathological changes are less characteristic.

Pathologically acute bronchiolitis may be divided into catarrhal and mural. The mural type may be further subdivided into simple, proliferative and destructive.

Pure catarrhal bronchiolitis as a distinct clinical entity is rare. Mural bronchiolitis is the usual reaction of the bronchioles to infection and is the type met with in measles, influenza, and pertussis. No definite demarcation line can be drawn between the three types of mural bronchiolitis; they merge gradually one into the other, and are probably different expressions of the same infection.

HISTOLOGY AND MORBID ANATOMY OF THE BRONCHIOLE

Before discussing the histological changes met with in acute bronchiolitis something should be said about the normal structure of the bronchiole.

(d) Lung: The bronchiolar inflammation stops at the beginning of the air spaces, which are usually collapsed but not infiltrated. In the cases of our series, there was no pneumonia. Pneumonia may, however, follow secondarily and is, indeed, predisposed to by the pulmonary collapse. In MacCallum's series there was usually pneumonia. His cases were, it must be remembered, in adults, and the changes are distinctly different in young children.

These pathological changes were described by MacCallum, Opie and MacNeil but the proliferative types described below were not recognized by them though they regularly occur in the bronchiolitis following measles, influenza and pertussis.

Proliferative bronchiolitis (fig. 6).—(a) Basal cells: These become rounder and may proliferate to such an extent that they may form a many-layered stratum. In some cases the epithelium is pushed to the centre of the lumen. This proliferation occurs only in the bronchioles. There is no apparent reason why mural bronchiolitis is sometimes proliferative and sometimes not.

(b) Epithelium: This is ordinarily of a low columnar type but it becomes elongated and may form a very high columnar epithelium. Instead of a single layer there may be several layers forming a sort of stratified epithelium.

Destructive bronchiolitis (fig. 7).—In one case both proliferative and destructive lesions were seen. There is complete destruction of epithelium. There is partial or complete destruction of the bronchiolar wall, with complete or partial loss of muscle and elastica. In the worst cases the bronchiole is converted into an abcess cavity. Sometimes this destruction is focal, part of the circumference of the wall only being destroyed.

The lumen contains detritus and polymorphs.

The air spaces adjacent to the bronchiole contain fibrin and enlarged alveolar cells are often seen; some attached, and others desquamated (cf. Giant cell pneumonia in measles, and influenza described by Opie).

The lung tissue is collapsed and there is no pneumonia though this may follow secondarily.

CAUSES OF DIFFERENCE IN REACTION

Proliferative changes are always present in the measles-influenza type but are absent in less specific infections.

Presumably the reaction of the bronchiole depends on two factors: (1) The nature of the infecting agent. · For instance, in MacCallum's post-measles cases, this was a hæmolytic streptococcus, which may produce severe changes in the bronchiolar wall. (2) The intensity of the toxin (whatever this may be). The toxin probably acts centrifugally from the lumen, and consequently becomes attenuated towards the periphery. A weak toxin may cause only epithelial changes, a moderately strong toxin—epithelial changes plus mural inflammation, with or without proliferative changes. A strong toxin causes destructive bronchiolitis, with less severe effects towards the periphery, due to attenuation of the toxin.

Another factor to be taken into consideration is the strength of the wall. The strong bronchial walls resist penetration, so that the inflammatory changes are confined to the mucous membrane. For example in the cases described by Goodpasture (1939), there was a destructive bronchiolitis, but in the bronchi there was no mural inflammation, though they were completely denuded of epithelium.

MORBID ANATOMY

The appearances may be characteristic. The lungs are usually congested. Scattered throughout are numerous tiny yellowish-white nodules, in the centre of which can be seen a bronchiole. The appearances may closely simulate those of miliary tuberculosis and may actually be indistinguishable to the naked-eye. There are also numerous bluish-grey areas of collapse and there may be scattered areas of emphysema

CLINICAL FEATURES

Bronchiolitis is chiefly met with in early childhood especially in the first three years. Cases may occur sporadically after measles, pertussis or influenza, or may arise independently of any of these diseases. The cases described in the paper of Engel and Newns (1940) were of the latter type, there being nothing to point to an infection with the influenza virus.

On the other hand a good example of an epidemic of acute bronchiolitis is that described by Hubble and Osborne (1941) during the influenza epidemic of 1940. They reported nearly 50 cases, 27 being under the age of 1 year. Seven died, all under the age of 2 years. These showed a definite mural bronchiolitis.

(2) *Mural.*—(*a*) The common feature of all forms of mural bronchiolitis is an infiltration of the walls of the bronchioles with monocytic cells, many of which are plasma cells. This results in an enormous thickening of the bronchiolar wall, which in some instances becomes almost as wide as the lumen of the bronchiole. This remarkable enlargement of the bronchiolar wall has deceived many into thinking that the infiltration is peribronchiolar. As can be seen in figs. 4 and 5, this is not the case.

(*b*) The epithelium may be loosened or cast off and may be seen as fragments within the lumen. Sometimes it is completely destroyed and no vestiges of it can be seen. Where there is proliferation of the basal cells, the epithelium may be pushed towards the centre of the lumen.

(*c*) Lumen: This is filled with cellular masses, monocytes and polymorphonuclears. The respiratory bronchioles may be filled with non-cellular mucoid material.
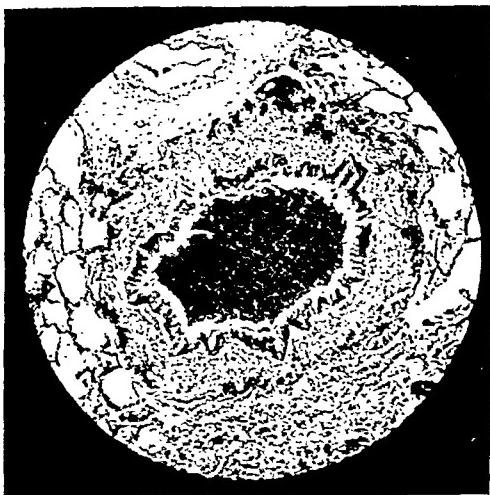
FIG. 4.—Bronchiole, from a child aged 5½ years, showing cellular infiltration of the wall—mural bronchiolitis. × 31.

FIG. 5.—Longitudinal section of a bronchiole, from a child aged 6 months, showing mural bronchiolitis. Note the striking infiltration of the wall and the exudate in the lumen. × 31.

FIG. 6.—Bronchiole from a child aged 5 years, showing proliferative mural bronchiolitis. Note the proliferation of the basal cells displacing the epithelium to the centre of the lumen. × 62.
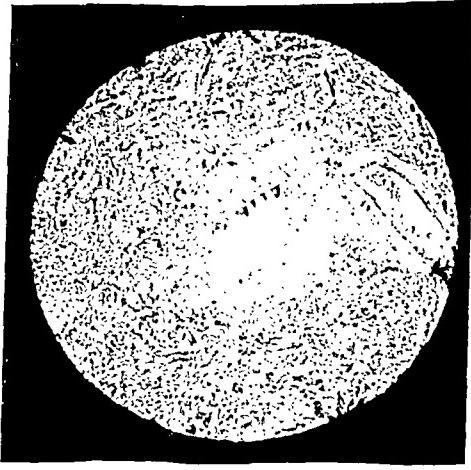
FIG. 7.—Bronchiole from a child aged 8 months, showing destructive bronchiolitis. The epithelium is destroyed and the wall is infiltrated with cells. The normal structure of the bronchiole is not discernible. The surrounding air spaces are collapsed. × 31.

Experimental work suggests that virus infection plays an important part in the production of acute bronchiolitis.

McCordock (1933) produced a typical mural bronchiolitis by the introduction of dilute vaccine virus into the trachea of rabbits. The superimposition of an infection by bacteria gave rise to a bronchopneumonia. In the experiments of Straub (1937) and of Nelson and Oliphant (1939), in which mice were infected with influenza virus, the main damage was in the bronchiolar epithelium, though there was some mural infiltration.

Goodpasture (1939) found inclusion bodies in epithelial cells in several of his cases of acute bronchiolitis in children, the oldest of which was 2½ years. Three cases followed measles, one pertussis, and the remaining one followed an unknown infection.

Much attention is being paid to virus pneumonias and it may very well be that these are much commoner than was formerly believed.

The evidence therefore suggests that a virus plays an important rôle in the causation of bronchiolitis. It is perhaps possible that mural bronchiolitis is a specific reaction of the lung to virus infection. In view, however, of the fact that secondary invaders of one kind or another are almost constantly found in the lung, a more likely possibility is that, as MacCallum suggests, the virus merely predisposes to a bacterial infection which latter is the actual cause of the bronchiolitis.

[For a more detailed account of proliferative mural bronchiolitis *see* Engel and Newns, 1940.]

REFERENCES

ENGEL, St., and NEWNS, G. H. (1940) *Arch. Dis. Child.*, **15**, 219.
GOODPASTURE, E., *et al.* (1939) *Amer. J. Dis. Child.*, **57**, 447.
HUBBLE, D., and OSBORNE, S. R. (1941) *Brit. med. J.* (i), 107.
MacCALLUM, W. G. (1919) The Pathology of the Pneumonia in the United States Army Camps. New York.
—— (1940) Textbook of Pathology. Rockefeller Institute for Medical Research, Philadelphia and London, monograph 10, p. 500.
McCORDOCK, H. A., and MUCKENFUSS, R. S. (1933) *Amer. J. Path.*, **9**, 221.
NELSON, A. A., and OLIPHANT, J. W. (1939) U.S. Publ. Hlth. Reps., **54**, 2044.
STRAUB, M. (1937) *J. Path. Bact.*, **45**, 75.

[June 3, 1944]

HELD AT HIGHWOOD HOSPITAL, BRENTWOOD

The Importance of Primary Pulmonary Tuberculosis

By J. V. HURFORD, M.D.

THOUGH a proportion of the accommodation is devoted to adolescent phthisis and to non-tuberculous lung conditions, Highwood Hospital is probably unique in the number of beds used for the treatment of primary tuberculosis.

A child in whom after investigation, a first infection has been diagnosed is given a period of bed-rest followed by graduated exercise with eventual discharge home or to an open-air school. The period in bed varies: in the younger child permission to get up is given if gland shadows are definitely smaller or calcified in the X-ray, erythrocyte sedimentation rate and temperature are normal and weight is satisfactory.

What is aimed at in taking the primary infection so seriously? What complications may be prevented? Some treatment is needed for the young child in whom a large primary complex alone may be a cause of ill-health. Hæmatogenous spread or meningitis are most to be feared within three to four months of infection, but we have had cases which demonstrated that that risk is never absent, before complete calcification has appeared. Atelectasis occurs more often under 5, and bronchiectasis is more likely to ensue in the younger age-group. Pleural effusion very often is interlobar, perhaps spanning a primary focus. On the costal site it is commoner at school age, and may come at any time up to eighteen months after the first infection (as may a bone and joint complication). There may be a massive non-specific reaction around a large primary focus, but acute bronchogenic spread is rather uncommon.

It may well be that by treating primary tuberculosis in an institution we reduce the number of children who would develop meningitis, atelectasis, pleurisy or some other complication. Do we prevent the development of adult or adolescent phthisis? Certain figures could be quoted to support this but no one has yet gone quite far enough and Sweany's work on the latent activity of calcified foci suggests that visible calcification is no criterion of healing. It is possible to have tubercle bacilli in stomach washings though calcification is proceeding in mediastinal glands. Doubtless, endogenous spread might occur from still caseous or from ��� ��ated "healed" glands, or from still active,

Catarrhal bronchiolitis is probably a rare syndrome" and is relatively benign though in very young infants it may be serious. The following case is probably an example of this condition:

A child of 2 years, said to have had pneumonia two weeks previously and to have been given M & B 693. On admission, there was slightly laboured breathing but no sign of obstructive dyspnœa and no cyanosis. The temperature was 101° but fell irregularly in the next few days. There was no dullness over the lungs but over the bases there were showers of moderate to fine crepitations. X-ray showed no localized opacity but there was a very fine diffuse mottling over both lungs. The crepitations persisted for over a week. The child made a complete recovery.

Sulphadiazine was given but it was doubtful whether it had any effect on the course of the disease.

Leucocytes : On admission 24,000—13,000 eight days later.

Mural bronchiolitis may start as a mild illness, with a tracheobronchitis, which after a few days is succeeded by more severe symptoms. More generally the child becomes severely ill within twenty-four to forty-eight hours. Grave symptoms develop, e.g. rapid respiration, high fever, dyspnœa, cyanosis, and severe prostration passing on to collapse. The characteristic symptom, and the one which gave rise to the term acute suffocative catarrh, is a severe obstructive dyspnœa. The infant seems to have the greatest difficulty in getting air into the lungs, and there is marked recession of the ribs.

After twenty-four to forty-eight hours there are numerous fine râles generally throughout both lungs, but no sign of consolidation, which only appears if pneumonia supervenes. There may be hyper-resonance due to emphysema.

The course of the disease is variable. Death may occur within two to three days, sometimes in an even shorter space of time, especially in young infants. Many cases, however, have a prolonged course and may die after two, three, or four weeks' illness. In these cases secondary pneumonia is usually present. In these prolonged cases miliary abscesses of the lungs are commonly met.

Recovery from the severe forms of bronchiolitis is infrequent especially in the younger infants.

DIAGNOSIS

This is easier in epidemics than in sporadic cases. The disease is usually confused with bronchopneumonia, with which in the more prolonged cases it gradually merges, though this may be an academic question since the treatment is the same. The differential diagnosis. is, however, important, since the prognosis is much worse in bronchiolitis, as it does not react to sulphonamide in the favourable way of cases of bronchopneumonia.

The absence of any signs of consolidation combined with the presence of generalized fine râles throughout both lungs are signs suggestive of bronchiolitis. The characteristic symptom of obstructive dyspnœa is also in favour of the latter diagnosis as opposed to that of bronchopneumonia. This symptom may be so severe that tracheal or laryngeal obstruction may be suspected.

An X-ray of the lungs may be helpful. The absence of any area of consolidation is against pneumonia. In many cases of bronchiolitis there may be nothing definitely abnormal in the X-ray. A diffuse fine mottling may be seen, however, often very faint, but sometimes so marked as to simulate very closely the appearances of miliary tuberculosis.

TREATMENT

This is unsatisfactory. As a rule bronchiolitis does not yield to sulphonamide therapy. The most useful therapeutic measure is the administration of oxygen, which is best given by means of an oxygen tent.

ÆTIOLOGY

The actual cause of bronchiolitis is by no means determined. It is usually a sequel of measles, pertussis or influenza. MacCallum in the measles epidemics in Army camps during the last war found in almost every case the hæmolytic streptococcus. He admits, however ("Textbook of Pathology", 1940), that this is "rather an unusual sequence of events since all of our cases in recent years have shown other bacteria, most often the Pfeiffer bacillus but always following a virus infection. It seems important to recognize the predisposing influence of the virus infection which makes possible the invasion of the bacteria and intensifies enormously their effects".

The possible rôle of the virus in the production of bronchiolitis can certainly not be left out of consideration. There are a number of pointers to its being an important factor.

Experimental work suggests that virus infection plays an important part in the production of acute bronchiolitis.

McCordock (1933) produced a typical mural bronchiolitis by the introduction of dilute vaccine virus into the trachea of rabbits. The superimposition of an infection by bacteria gave rise to a bronchopneumonia. In the experiments of Straub (1937) and of Nelson and Oliphant (1939), in which mice were infected with influenza virus, the main damage was in the bronchiolar epithelium, though there was some mural infiltration.

Goodpasture (1939) found inclusion bodies in epithelial cells in several of his cases of acute bronchiolitis in children, the oldest of which was 2½ years. Three cases followed measles, one pertussis, and the remaining one followed an unknown infection.

Much attention is being paid to·virus pneumonias and it may very well be that these are much commoner than was formerly believed.

The evidence therefore suggests that a virus plays an important rôle in the causation of bronchiolitis. It is perhaps possible that mural bronchiolitis is a specific reaction of the lung to virus infection. In view, however, of the fact that secondary invaders of one kind or another are almost constantly found in the lung, a more likely possibility is that, as MacCallum suggests, the virus merely predisposes to a bacterial infection which latter is the actual cause of the bronchiolitis.

· [For a more detailed account of proliferative mural bronchiolitis *see* Engel and Newns, 1940.]

<div align="center">REFERENCES</div>

ENGEL, St., and NEWNS, G. H. (1940) *Arch. Dis. Child.*, **15**, 219.
GOODPASTURE, E., *et al.* (1939) *Amer. J. Dis. Child.*, **57**, 447.
HUBBLE, D., and OSBORNE, S. R. (1941) *Brit. med. J.* (i), 107.
MacCALLUM, W. G. (1919) The Pathology of the Pneumonia in the United States Army Camps. New York.
—— (1940) Textbook of Pathology. Rockefeller Institute for Medical Research, Philadelphia and London, monograph 10, p. 500.
McCORDOCK, H. A., and MUCKENFUSS, R. S. (1933) *Amer. J. Path.*, **9**, 221.
NELSON, A. A., and OLIPHANT, J. W. (1939) U.S. Publ. Hlth. Reps., **54**, 2044.
STRAUB, M. (1937) *J. Path. Bact.*, **45**, 75.

<div align="center">[June 3, 1944]</div>

<div align="center">HELD AT HIGHWOOD HOSPITAL, BRENTWOOD</div>

The Importance of Primary Pulmonary Tuberculosis

<div align="center">By J. V. HURFORD, M.D.</div>

THOUGH a proportion of the accommodation is devoted to adolescent phthisis and to non-tuberculous lung conditions. Highwood Hospital is probably unique in the number of beds used for the treatment of primary tuberculosis.

A child in whom after investigation, a first infection has been diagnosed is given a period of bed-rest followed by graduated exercise with eventual discharge home or to an open-air school. The period in bed varies: in the younger child permission to get up is given if gland shadows are definitely smaller or calcified in the X-ray, erythrocyte sedimentation rate and temperature are normal and weight is satisfactory.

What is aimed at in taking the primary infection so seriously? What complications may be prevented? Some treatment is needed for the young child in whom a large primary complex alone may be a cause of ill-health. Hæmatogenous spread or meningitis are most to be feared within three to four months of infection, but we have had cases which demonstrated that that risk is never absent . before complete calcification has appeared. Atelectasis occurs more often under 5, and bronchiectasis is more likely to ensue in the younger age-group. Pleural effusion very often is interlobar, perhaps spanning a primary focus. On the costal site it is commoner at school age, and may come at any time up to eighteen months after the first infection (as may a bone and joint complication). There may be a massive non-specific reaction around a large primary focus, but acute bronchogenic spread is rather uncommon.

It may well be that by treating primary tuberculosis in an institution we reduce the number of children who would develop meningitis. atelectasis, pleurisy or some other complication. Do we prevent the development of adult or adolescent phthisis? Certain figures could be quoted to support this but no one has yet gone quite far enough and Sweany's work on the latent activity of calcified foci suggests that visible calcification is no criterion of healing. It is possible to have tubercle bacilli in stomach washings though calcification is proceeding in mediastinal glands. Doubtless. endogenous spread might occur from still.caseous or from ~·· ·ated "healed" glands. or from still active,

FIG. 1 (*Case I*).—J. B. Shows primary focus in 1st intercostal space on right, with only centre calcified. Scar of post-primary lesion in 2nd intercostal space.
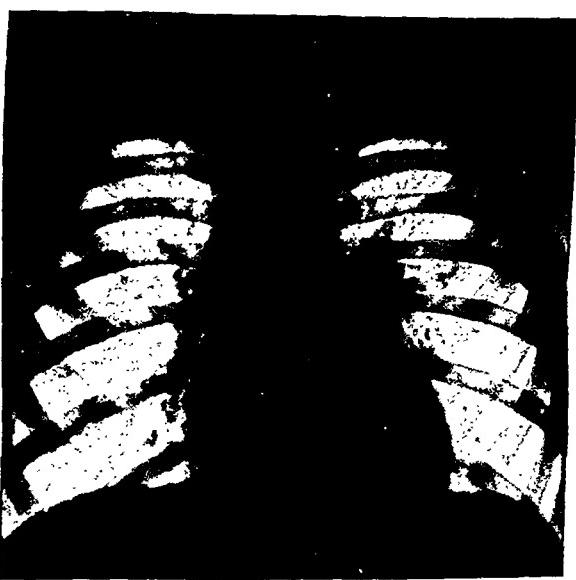
FIG. 2 (*Case II*).—R. F. Shows calcification in left hilar region. Enlarged gland still visible (before discharge from hospital in January 1942).
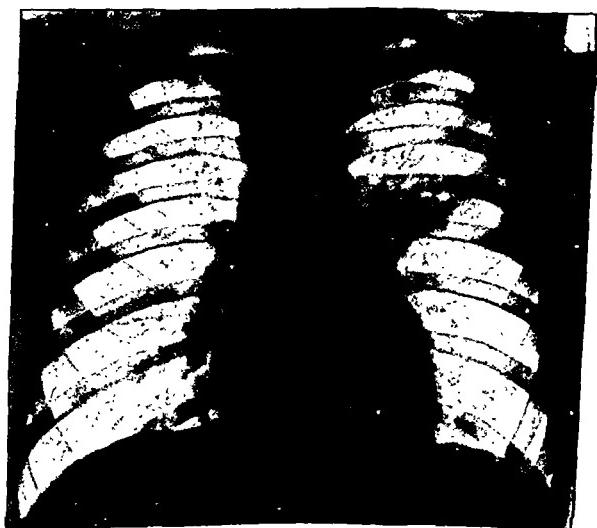
FIG. 3 (*Case II*).—R. F. Parenchymatous extension of disease beyond hilum (return to hospital in August 1942)
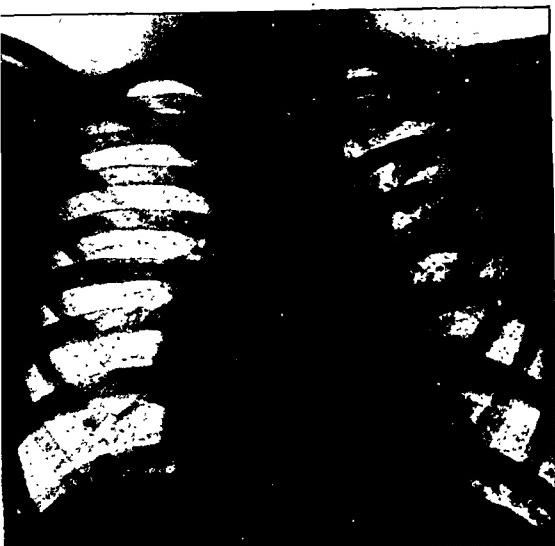
FIG. 5 (*Case IV*).—J. D. Enlarged (partially calcified) bilateral hilar glands. Infiltration left base.

FIG. 6 (*Case IV*).—J. D. (Lateral film taken on same date as fig. 5.) Enlarged hilar glands with cavity visible just below them.
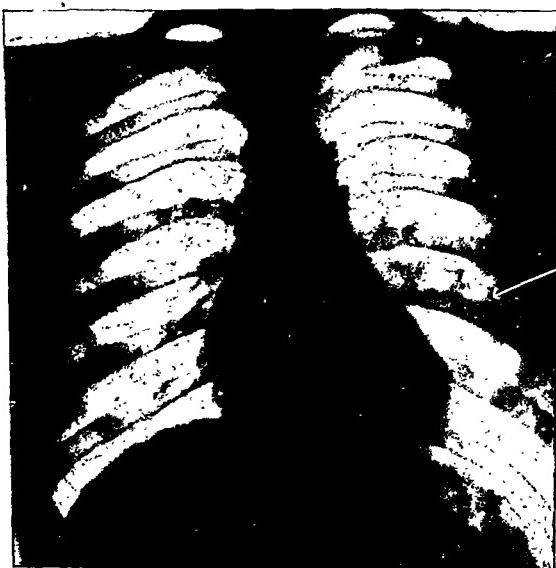
FIG. 4 (*Case III*).—E. B. Limited infiltration with formation of small cavity in left lower lobe (arrow). Enlarged left hilar gland (more obvious in other films).

though apparently calcified Ghon or Simon's foci. In certain cases among adolescents there is a suggestion that the interval between primary infection and post-primary disease has been very short. In fig. 1 (Case I, J. B.) a focus can be seen in the first right intercostal space; there is central calcification surrounded by a caseous ring. Previous X-rays had shown bronchogenic spread in the second space.

CASE II.—R. F. (figs. 2 and 3), boy, aged 13. Contact of grandparents who died of tuberculosis before his admission in 1940. Left Highwood in January 1942 (fig. 2) but began to lose weight and was readmitted in August 1942 (fig. 3). No fresh contact whilst out of hospital. Such a case indicates centripetal spread from apparently calcified hilar shadows.

The next case is representative of a group in which a still active primary infection (shown by enlarged glands) is complicated by a small post-primary infiltration.

CASE III.—E. B. (fig. 4), girl, aged 13½. No family history. Onset with erythema nodosum and hæmoptysis. Sputum positive on one occasion and tubercle bacilli in a swab taken on bronchoscopy. Treated by left artificial pneumothorax.

CASE IV.—J. D. (figs. 5 and 6), boy, aged 12. The large glands showed calcification but it was not till six months after admission that bronchogenic spread became definite and a cavity appeared. He had no history of contact and his illness was ushered in with slight cough, loss of weight and lassitude.

I think such cases are rather unusual, as the young adolescent so often has a "guinea-pig-like" reaction to the adult type of disease. Apart from their obvious difficulties in exact diagnosis, perhaps they hint at the importance of not disregarding primary tuberculosis at that age (or after it—if general experience with "unsalted" hospital nurses is any guide!).

To go back to the earlier part of this paper, whilst there is something to be said for treating clinically, obvious primary tuberculosis in special hospital or preventorium, the drawbacks should be mentioned: exposure to cross-infection (with some tendency to exacerbation of disease), interruption of normal schooling (the hospital school though invaluable, is not a proper substitute) and prolonged hospitalization of the child in its formative years.

Treatment of Pulmonary Tuberculosis in Children

By T. Holmes Sellors, M.Ch.

In any discussion on tuberculosis in children we must include a small but definite group who are affected by the typical adult form of the disease with parenchymatous infiltration, ulceration and cavitation. This is quite apart from the primary class of lesion and its immediate sequelæ. The "adult" type of disease may occur in children as young as 5 or 7 years, but most of the cases are recognized a few years later and merge into the numerically larger age-group of the young adolescent.

The features of the condition in children are largely dominated by the instability of the actual pulmonary lesions. Rapid cavitation, which is probably of distension type in many instances, appears with little warning and bronchogenic dissemination occurs even when adequate control seems to be established. It more or less follows that the average prognosis is poor, though strict sanatorium treatment coupled with appropriate collapse measures can give good results.

As is now widely recognized the general appearance of the patient is little indication of the degree of involvement in the lung fields. Children with extensive disease can look extremely robust and healthy, especially if they have been held under strict conditions of treatment. Girls tend to be well developed and mature, but in the long run do less well than boys. Terminal or toxic cases naturally do not give this false impression, but show the traditional features of phthisis.

Sanatorium régime for children has several special points that must be observed. First, there is the insistence on complete bed-rest over a much longer period than might be needed for the adult: the child who is out of bed cannot be satisfactorily controlled and rested, and it is consequently important to err on the side of caution. Secondly, there is the need for diversion and educational facilities, and it is noticeable what a relatively high standard of knowledge is attained when a teaching staff such as is employed at Highwood and other large children's sanatoria is available. The high standard of morale and general contentment is a further indication of satisfactory conditions of treatment.

Cough and sputum have certain differences from these features in adults. Children can undoubtedly cough and splash in a manner that is difficult to control, but the

exhibition of sputum is usually delayed until the child is anything up to 7, 8 or 9 years. Until expectoration is obtained sputum examination for tubercle bacilli has to be done through gastric lavage with the additional help of culture and guinea-pig inoculation. The presence of "open" cases in a youthful community leads to problems in segregation which are much more important than in an adult sanatorium, for example.

As regards the employment of collapse therapy or surgery in the phthisical child, all the procedures that are available in the adult can be applied to children with one exception—namely thoracoplasty. Surgical tradition is against the use of extensive rib resection in growing children on account of the extreme scoliosis and deformity that results as the child increases in stature.

Artificial pneumothorax is the most valuable collapse measure and it is often employed at a much earlier stage than would be considered suitable in adults. This is a question of expediency rather than choice and it may have a dramatic effect in reducing fever and improving the general condition. In spite of the tendency to early use of artificial pneumothorax effusions are not as common as might be expected, though re-expansion and obliteration may occur quickly and call for careful control. Thoracoscopy, in which the ordinary adult instrument can be safely used, is a valuable supplement to pneumothorax treatment and helps to complete the collapse and healing of many areas of cavitation.

The indications for phrenicectomy are as indefinite as they are in adults though there is a natural tendency to keep to the crush or temporary paralysis rather than to produce irrevocable loss of function in the hemi-diaphragm of a young child. A tribute to the training and morale of even the youngest patients lies in the fact that these operations are undertaken with local anæsthesia with a great deal less fuss than may occur with many adults. Pneumoperitoneum used in conjunction with a one-sided phrenic paralysis has not been persisted with long enough to assess its final value in children. The early stages are not so well tolerated as in older patients, but the elevation of diaphragm obtained is so extensive in some cases that the procedure demands careful consideration as a collapse measure. In the absence of thoracoplasty and if other methods fail this combined manœuvre will have to be given a thorough trial.

Cavity drainage has proved valuable in a few cases but the difficulty has been to maintain the obliteration of the cavity after the suction drainage has been stopped. In the adult a limited thoracoplasty usually proves successful, but at present we do not feel that this is practicable in children. What sometimes happens is that a child of 14 to 15 years has reached such an advanced state of physical growth and maturity that thoracoplasty becomes a practical proposition by the time drainage treatment has been prolonged to its limits. However, if this does not appear likely, attempts to maintain closure by phrenicectomy and pneumoperitoneum may be considered.

Extrapleural pneumothorax has had a limited application and some success has been achieved in cases of pneumothorax failure and in which apical collapse cannot be attained by other methods. The difficulty has proved to be maintenance of the extrapleural space and prevention of too early lung expansion. Even most assiduous care and persistence with refills is not enough to prevent obliteration of the space earlier than is desired.

Treatment therefore in this special class of case follows the same lines as in adults with minor modifications, but the important thing to realize is that these patients can and should be treated and not left to form an obscure and neglected group. Admittedly it is difficult to distinguish between some of the primary manifestations of the disease and the later phases of activity, but careful observation and radiological examination of suspect cases should do much to prevent the disease progressing too far and too fast before treatment can be instituted.

Bronchial Obstructions in Primary Pulmonary Tuberculosis

By W. F. RICHARDS, M.B.

BRONCHIAL obstruction in childhood tuberculosis is a common complication, especially in younger children.

In a recent survey of cases admitted to this hospital we found that among 239 children under 6 years old suffering from primary tuberculosis of the lungs 50 or 21% developed a sector or lobar collapse due to bronchial obstruction.

Above this age, the incidence of this complication was less, for instance—7% of 114 children whose ages ranged from 6 to 9 years, and 6.5% of 92 children over 10.

though apparently calcified Ghon or Simon's foci. In certain cases among adolescents there is a suggestion that the interval between primary infection and post-primary disease has been very short. In fig. 1 (Case I, J. B.) a focus can be seen in the first right intercostal space; there is central calcification surrounded by a caseous ring. Previous X-rays had shown bronchogenic spread in the second space.

Case II.—R. F. (figs. 2 and 3), boy, aged 13. Contact of grandparents who died of tuberculosis before his admission in 1940. Left Highwood in January 1942 (fig. 2) but began to lose weight and was readmitted in August 1942 (fig. 3). No fresh contact whilst out of hospital. Such a case indicates centripetal spread from apparently calcified hilar shadows.

The next case is representative of a group in which a still active primary infection (shown by enlarged glands) is complicated by a small post-primary infiltration.

Case III.—E. B. (fig. 4), girl, aged 13½. No family history. Onset with erythema nodosum and hæmoptysis. Sputum positive on one occasion and tubercle bacilli in a swab taken on bronchoscopy. Treated by left artificial pneumothorax.

Case IV.—J. D. (figs. 5 and 6), boy, aged 12. The large glands showed calcification but it was not till six months after admission that bronchogenic spread became definite and a cavity appeared. He had no history of contact and his illness was ushered in with slight cough, loss of weight and lassitude.

I think such cases are rather unusual, as the young adolescent so often has a "guinea-pig-like" reaction to the adult type of disease. Apart from their obvious difficulties in exact diagnosis, perhaps they hint at the importance of not disregarding primary tuberculosis at that age (or after it—if general experience with "unsalted" hospital nurses is any guide!).

To go back to the earlier part of this paper, whilst there is something to be said for treating clinically obvious primary tuberculosis in special hospital or preventorium, the drawbacks should be mentioned: exposure to cross-infection (with some tendency to exacerbation of disease), interruption of normal schooling (the hospital school though invaluable, is not a proper substitute) and prolonged hospitalization of the child in its formative years.

Treatment of Pulmonary Tuberculosis in Children

By T. Holmes Sellors, M.Ch.

In any discussion on tuberculosis in children we must include a small but definite group who are affected by the typical adult form of the disease with parenchymatous infiltration, ulceration and cavitation. This is quite apart from the primary class of lesion and its immediate sequelæ. The "adult" type of disease may occur in children as young as 5 or 7 years, but most of the cases are recognized a few years later and merge into the numerically larger age-group of the young adolescent.

The features of the condition in children are largely dominated by the instability of the actual pulmonary lesions. Rapid cavitation, which is probably of distension type in many instances, appears with little warning and bronchogenic dissemination occurs even when adequate control seems to be established. It more or less follows that the average prognosis is poor, though strict sanatorium treatment coupled with appropriate collapse measures can give good results.

As is now widely recognized the general appearance of the patient is little indication of the degree of involvement in the lung fields. Children with extensive disease can look extremely robust and healthy, especially if they have been held under strict conditions of treatment. Girls tend to be well developed and mature, but in the long run do less well than boys. Terminal or toxic cases naturally do not give this false impression, but show the traditional features of phthisis.

Sanatorium régime for children has several special points that must be observed. First, there is the insistence on complete bed-rest over a much longer period than might be needed for the adult: the child who is out of bed cannot be satisfactorily controlled and rested, and it is consequently important to err on the side of caution. Secondly, there is the need for diversion and educational facilities, and it is noticeable what a relatively high standard of knowledge is attained when a teaching staff such as is employed at Highwood and other large children's sanatoria is available. The high standard of morale and general contentment is a further indication of satisfactory conditions of treatment.

Cough and sputum have certain differences from these features in adults. Children can undoubtedly cough and splash in a manner that is difficult to control, but the

The majority of our cases that were bronchoscoped showed a slit-like or crescent-shaped constriction of the affected bronchus, which suggested that obstruction was due to extrabronchial pressure by an enlarged bronchopulmonary lymph gland. But in a large number there was a soft concentric stenosis formed by an annular swelling of the mucosa, pointing to a local inflammatory process seated possibly in the submucosal lymphatics of the bronchus. In three cases the disease had ulcerated through, and granulations were found in the lumen. A number of long-standing cases showed deformed
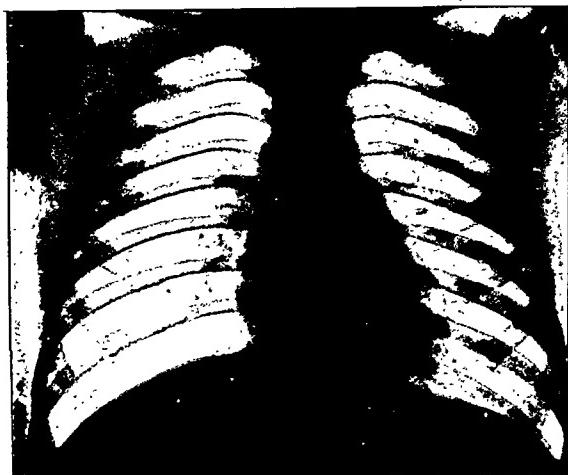
FIG. 11 (*Case IV*).—During inspiration. Showing emphysema of right lung.
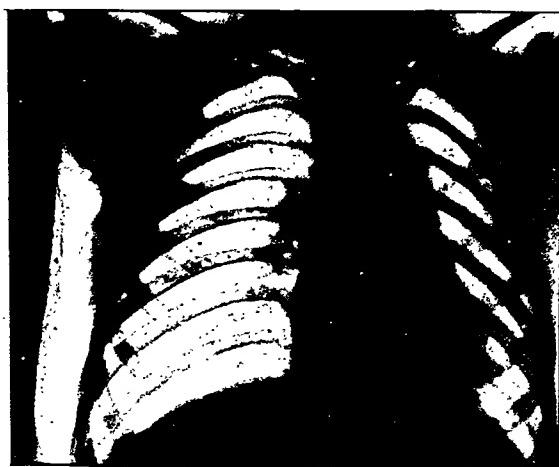
FIG. 12 (*Case IV*).—During expiration. Shift of heart to left and descent of right diaphragm.

bronchial openings, rectangular or triangular in shape above a funnel-shaped rigid stenosis.

In our series the right middle bronchus was affected most frequently, 23 times out of a total of 66 affected lobes. Then came the right lower lobe or right basal bronchi with 13. The right and left upper lobes were equally involved with 9 collapses each, and left middle lobe or lingula, and left base were both affected in 6 cases. Four children had more than one lobe affected.

AUG. DIS. IN CHILD.—2

The larger incidence among younger children is due almost certainly to the greater enlargement of the bronchopulmonary glands that takes place at this age, as a result of the tuberculous infection.

I have found no figures in the literature on this subject comparable with ours. In fact bronchial obstruction from this cause—primary tuberculosis—seems to be treated as a comparatively rare complication. For instance, from the Department of Pediatrics at the Harvard Medical School 15 cases of bronchial obstruction due to primary tuberculosis were reported from material collected over a period of eleven years. Spivek in America thought a series of 18 cases worth reporting.
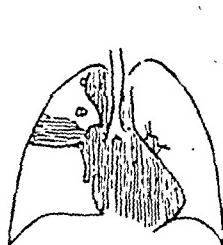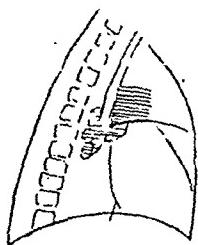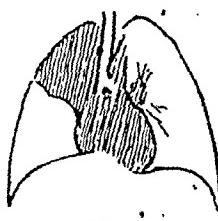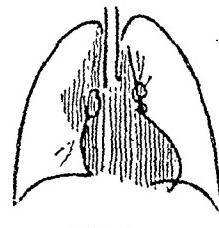
FIG. 1.   FIG. 2.   FIG. 3.   FIG. 4.

FIG. 1 (*Case I*).—March, 1943. Wedge-shaped area of collapse. Above this a primary focus is visible.
FIG. 2 (*Case I*).—Right lateral. Shows characteristic quadrilateral shadow.
FIG. 3 (*Case I*).—November, 1943. Whole of right upper lobe has collapsed.
FIG. 4 (*Case I*).—April, 1944. Re-expansion of right upper lobe almost complete.
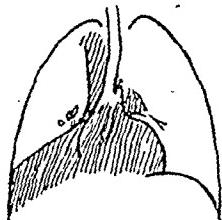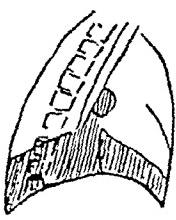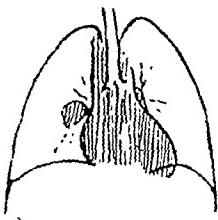
FIG. 5.   FIG. 6.   FIG. 7.

FIGS. 5 and 6 (Right lateral) (*Case II*).—Show collapse of right middle lobe and all three basic sectors of right lower lobe.
FIG. 7 (*Case III*).—February, 1943. Shows enlarged glands at right hilum.
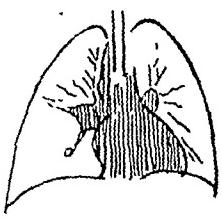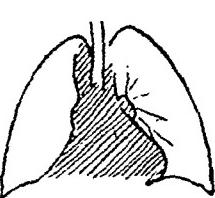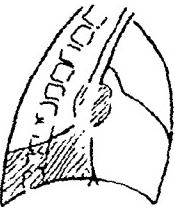
FIG. 8.   FIG. 9.   FIG. 10.

FIG. 8 (*Case III*).—April, 1943. Emphysema of right base.
FIG. 9 (*Case III*).—August, 1943. Collapse at right base.
FIG. 10 (*Case III*).—Right lateral. Shows collapse of right middle and posterior basic sectors.

Pathology.—Chevalier Jackson has typed bronchial obstruction as: (1) The bypass valve producing wheezy respiration; (2) the check valve producing emphysema; and (3) the stop valve producing collapse of the lung distal to it.

Although a history of noisy breathing or wheezing can be obtained from parents in some cases, the vast majority are diagnosed in the third stage. I remember seeing only four good examples of the check valve. These check valve cases are apt to be diagnosed and treated as asthmatics. Their symptoms and physical signs strongly suggest this diagnosis (Faust, 1936); 11 of 15 cases reported from the Harvard Medical School previously referred to had wheezing or loud breathing as a symptom (Meneghello and Smith, 1943).

Section of Epidemiology and State Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., D.M., F.R.C.P.

[*June* 23, 1944]

The Measurement of Morbidity

By PERCY STOCKS, M.D., D.P.H.

BEFORE we can measure anything two conditions are necessary, a definition of what it is that we are measuring and a scale of measurement. These conditions are not so easy of fulfilment for morbidity as for mortality. In a highly civilized community in times of peace there is little difficulty in deciding whether a person is alive or dead; and well tried scales by which to measure the causes of death have been in existence for a long time. Changes in these scales are made from time to time, but even when such changes are fundamental in character, as in the 1940 revision of the basis of the national statistics of England and Wales, it is still possible to convert one scale to another with considerable accuracy. Neither of these conditions holds good for morbidity measurement, for in the first place the dividing line between illness and health is often indefinite, thus adding another dimension of variability. Examples of this are to be seen in the varying response of different individuals to infection by certain organisms, a state of immunity equilibrium being reached in some cases without any apparent departure from health, whereas in others the process is accompanied by a period of acute illness. In some persons objective signs thought to indicate pathological change may be unaccompanied by subjective symptoms, sometimes because they are confused with physiological changes or are variations which fall within the normal range. Examples of this have been seen in adolescent goitre, orthostatic albuminuria and infantile rickets.

In the second place the dividing line between different types of illness usually tends to be less distinct in the earlier than in the later stages, and in milder forms of disease than in more fatal forms. Consequently the classification of illnesses of all grades of severity involves more difficulty than does the classification of fatal illnesses alone. This may be the reason why the compilation of a standard classification of diseases and injuries arranged for the purposes of morbidity measurement was awaited for so long. It was always in the minds of those who met together at decennial intervals to revise the International List of Causes of Death that a parallel list for morbidity statistics was needed, but after general discussion it was postponed for further consideration at the next revision. In the meantime different lists were employed for the purposes of military statistics of disease, pensions and health insurance. Scotland has used a short list of diseases in the useful series of reports on incapacitating sickness in the insured population, but the content of the groups and rules of selection where more than one disability was present are not very clearly defined. Canada was, I think, the first country to compile and use a national classification based upon the International List, 1929 revision, and the reports on the incidence of illness in the Canadian Civil Service have reached a high standard in morbidity recording.

In 1933 the first edition of the American Standard Nomenclature of Disease was published, a coded and classified nomenclature which was mainly the work of Dr. H. B. Logie. This was adopted in some of our large hospitals for the purposes of card-indexing the diseases and complications observed in the patients treated. For that purpose the Standard Nomenclature, of which an improved 3rd edition was published in 1942, is admirable. Its coding system consists of three digits denoting the topographical classification followed by three or four more digits denoting the ætiology, and it enables the research worker on any particular disease or injury to assemble the records and analyse them. This method of investigation is, of course, very fruitful, but if it were the only method of statistical study of morbidity the field of social medicine would be limited indeed. There is another and entirely different method of approach which has proved its usefulness in the past in the study of mortality, namely, first to assemble statistics of broad groups of diseases, break them down according to sex, age, occupation, marital condition, place of residence and so on, and look for significant relations with these factors. If any such are indicated, the broad group is then subdivided into the constituent diseases in order to discover which are responsible for the observed trends and which are not, and thus may be brought to light unsuspected facts about ætiology. In order to apply this method large numbers are essential in the first instance, because the breakdown by sex, age and other social factors necessitates sorting into so many compartments. Moreover, if the whole field of morbidity is to be studied in this way the

CASE I.—An example of sector collapse in the right upper lobe in a child aged 2 (figs. 1 and 2). The whole upper lobe became atelectatic seven and a half months after admission (fig. 3). Eventually the collapsed areas re-expanded spontaneously (fig. 4).

CASE II.—A child of 3 years of age with obstruction of the right descending bronchus by tuberculous granulation tissue, resulting in collapse of the basal sectors of his right lower lobe, and middle lobe with gross bronchiectasis. Bronchoscopy established drainage and alleviated a hectic temperature (figs. 5 and 6).

CASE III.—A 2-year-old child with enlarged hilum and bronchopulmonary glands in the right (fig. 7), who successively developed emphysema, collapse and finally re-expansion in the right posterior and middle basic sectors (figs. 8, 9 and 10). Bronchoscopy revealed the cause of obstruction to be an enlarged gland situated at the bifurcation of the middle and posterior basic bronchi.

CASE IV.—A 6-year-old boy with emphysema of the right lung produced by tuberculous granulation tissue in the right bronchus. In this case the heart swung away from the emphysematous area during expiration and the right diaphragm descended during this phase of respiration (figs. 11 and 12). Granulations were removed at bronchoscopy and an X-ray taken the next day showed no sign of emphysema.

As regards the more immediate prognosis of bronchial obstruction in these cases: 32 or half of our series of 64 cases re-expanded their collapse without incident. The shortest time from collapse to spontaneous re-expansion was one month, the longest while under observation was two years. 10 of the 64, or 15·6%, developed bronchiectasis; the right middle lobe accounting for six of the latter. 22, or 34·4%, still had their collapse on discharge.

SUMMARY

Bronchial obstruction is a common complication of primary lung tuberculosis, especially in children under 6 years old. In the majority it is caused by pressure on a bronchus from an enlarged lymph gland. But obstruction from bronchial tuberculosis is not uncommon in children.

REFERENCES

FAUST, O. A. (1936) *Amer. J. Dis. Child.*, 51, 118-122.
JACKSON, CHEVALIER, and JACKSON, CHEVALIER L. (1934) Bronchoscopy, Esophagoscopy, and Gastroscopy. Philadelphia and London.
MENEGHELLO, J., and SMITH, C. A. (1943) (From Dept. Pediatrics Harvard Med. Sch.) *J. Pediat.*, 22, 265-285.
SPIVEK, M. L. (1936) *Amer. J. Dis. Child.*, 51, 69-83.

NOTIFICATION AS A MEASURE OF MORBIDITY

RATIO OF NOTIFICATIONS TO DEATHS ——   CRUDE DEATH RATE (D) - - - -
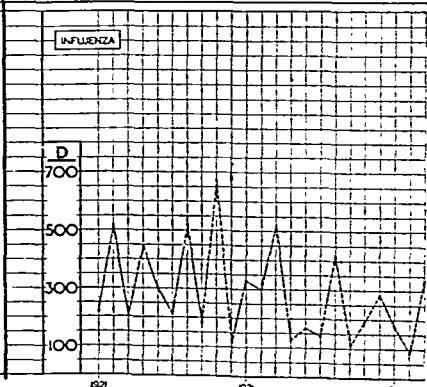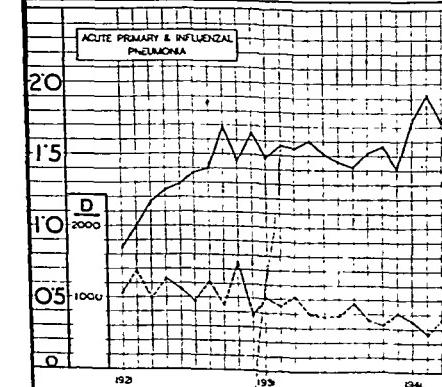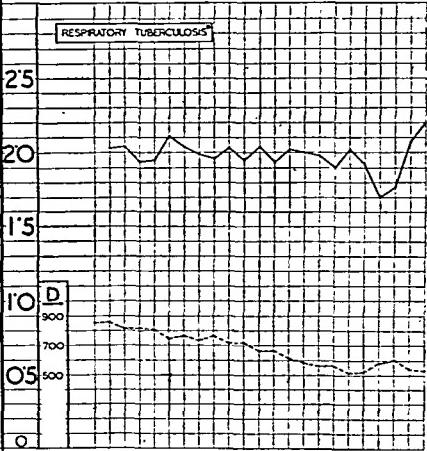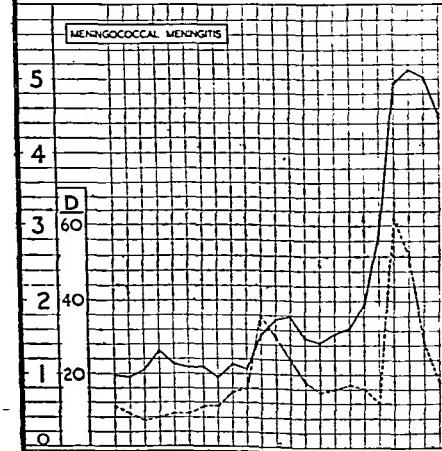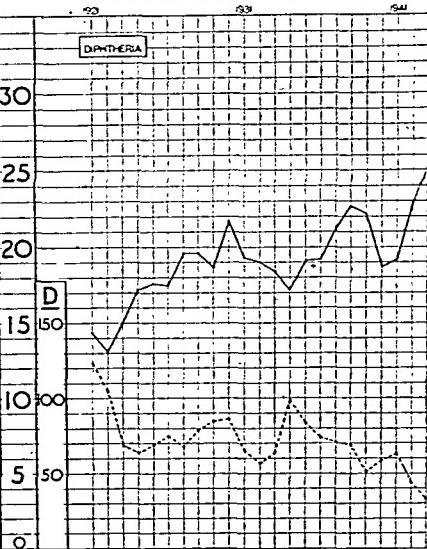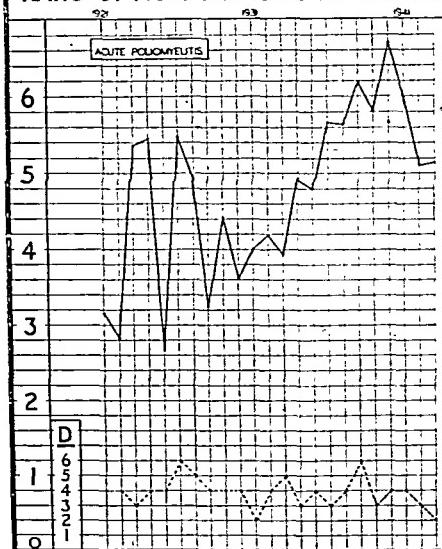
* RATIO OF NOTIFICATIONS IN (CURRENT YEAR + TWICE PRECEDING YEAR + SUM OF 2ND AND 3RD YEARS BACK) TO 5 TIMES DEATHS OF NOTIFIED PERSONS IN CURRENT YEAR.

magnitude of the tabulating processes demands that we start with a manageable number of disease groups and proceed later to examine in more detail those portions of the tabulation which seem to show peculiarities. This means that we must start with a short list of disease groups which have due regard to public health interests on the one hand and to supposed common ætiology on the other, and which can be readily resolved into their constituent disease components for further analysis. It is at this point that the American Standard Classification fails to meet our requirements, for it is impracticable to assemble together all the 6-figure code numbers from different parts of the list to produce such groups as upper respiratory infections, cancer, anæmias, intracranial lesions of vascular origin, primary pneumonias, and hernia. No one, so far as I am aware, has succeeded in producing comprehensive tabulations of morbidity by means of the Classification, for it was not designed for that purpose.

This was realized in America some years ago and two provisional classifications were prepared, one by the Welfare Council of New York for hospital statistics which has been used in their recently published Hospital Discharge Study, the other by the United States Public Health Service and Vital Statistics Division of the Census Bureau which is now in process of revision and completion. The latter is based upon the framework of the International List of Causes of Death, but not the former. We were, perhaps, fortunate in this country in having a clear field when the Oxford, Berks and Bucks Regional Council of the Nuffield Provincial Hospitals Trust and the Editorial Board for the Official Medical History of the War each arrived at the conclusion that an urgent need for a standard classification for statistics of morbidity had arisen. The sequel was the appointment of a Committee of the Medical Research Council to prepare one, and during most of the time occupied by its preparation the list was subjected to a searching test by applying it to many thousands of in-patient records from E.M.S. hospitals. By this means defects were discovered and remedied, not only in the grouping of diseases and injuries but also in the system of rules whereby primary and contributory conditions were to be distinguished. This Classification has now been published, and has been adopted as the basis of morbidity statistics not only for the E.M.S. hospitals and the Nuffield Bureaux of Sickness Records but also, in condensed forms, by the Ministry of Pensions, the Industrial Health Research Board and some of the Middlesex municipal hospitals. We now have, therefore, a measuring scale for the subdivision of morbidity, and I shall devote most of this paper to some examples of its use, and to a discussion of the other difficulty to which I have referred, namely, the dividing line between illness and health.

NOTIFICATION AND MORTALITY STATISTICS

Certain diseases of special hygienic significance are required to be notified to the public health authority in order that the necessary action may be taken, and the numbers of such notifications have for long provided a means of measuring trends of incidence. This measure is subject to a number of fallacies of which most of us are well aware. One is the variability of the dividing line between reactions to infection which are so slight or atypical as not to be recognized or thought definite enough to be notified and those which are thought to constitute the disease entity which the doctor is instructed to notify. During an epidemic or through increasing attention being directed in the medical press or by the public health authority to slight and atypical manifestations of infection by a particular organism or virus, notifications may increase for a time and then fall again as interest wanes. Fig. 1 shows two probable examples of this, namely, the continued rise in the ratio of notifications to deaths for acute poliomyelitis between 1930 and 1940, and the sudden increase in the ratio for meningococcal meningitis which accompanied and outlasted the 1931 exacerbation in the death-rate from that disease. For some diseases the decision to notify is often made because it is a necessary prelude to removing the patient to hospital, and direct encouragement to send doubtful cases to hospital in order to secure more rapid diagnosis and treatment was probably responsible for the rapid increase in the ratio of notifications to deaths for diphtheria in the period 1934 to 1938, as shown by the diagram.

This incentive to notify also operates in the case of tuberculosis, but in this case there are often strong incentives not to notify slight cases for whom institutional treatment is not desired and who can be treated privately. Correlation of notifications with death certificates for respiratory tuberculosis shows that about 10% of persons dying of the disease escape notification. This disease has been included on the diagram to demonstrate two points: (1) that the ratio of notifications to deaths of notified persons after a time-lag appropriate to the rate of dying oscillated about a mean level of 2 and showed no consistent change between 1922 and 1938, notwithstanding the continuous decline in notifications and deaths; (2) that the rapid oscillations corresponded inversely with those of the influenza death-rate. In other words the only important factor disturbing the

tics of 1944. For this reason the former·plan·of working by date of admission was adopted notwithstanding the disadvantages entailed by time-lag. In practice the statistics are closed after a year has elapsed from the end of the period and provisional figures free from appreciable error can be tabulated at the end of nine months whilst approximate figures for some diseases can be obtained after shorter periods.

·This has made possible the study of the incidence curves of influenza and some related acute conditions during the recent epidemic shown in fig. 2. Three of the graphs show the estimated numbers of patients admitted from the Services to all E.M.S. hospitals during each week, from August to mid-January in the upper part of the diagram and to·the end of February in the lower part, with a diagnosis of influenza (M.R.C. Nos. 070, 071, 073), coryza (No. 072) and acute sore throat (Nos. 481, 482). The fourth graph shows, on' a scale at the right hand of the diagram arbitrarily chosen so as to bring the peaks to about the same height, the weekly influenza deaths in the great towns of England and Wales. The two parts of the diagram compare corresponding weeks in 1942-43 and 1943-44.

In the autumn and winter of 1942-43 when influenza deaths showed a·normal seasonal trend, influenza admissions increased from about 50 per week in the autumn to about 240 per week in January. Milder catarrhs not described as influenza showed a corresponding January maximum, the weekly averages in successive months from August to February being about 5, 9, 12, 25, 35, 80, 45. Admissions for acute sore throat increased from about 120 per week in August to 210 in November-December and 200 in January, falling to 155 in February. In the autumn and winter of 1943-44 influenza admissions showed no excess over corresponding weeks of the previous year until the second week of October when the weekly number began to rise from about 40, reaching a peak of 875 in the last week of November. Deaths in the great towns increased at much the same rate with a time-lag of three weeks between the graphs. Admissions for milder catarrhs were also at a much higher level than a year earlier and they also reached their maximum in the last week of November. Acute sore throat admissions in successive months from August to December averaged about 150, 150, 160, 145, 100 per week, the incidence being apparently quite unaffected by the influenza epidemic, an interesting fact.

The card record system at Norcross has been so designed that if a patient is transferred from one E.M.S. hospital to another or to a convalescent depot, or is readmitted for the same complaint within a week of discharge, all the hospital records are brought together and count in the statistics as one illness only. This eliminates a defect which often mars aggregated civilian hospital statistics, since some patients are admitted in turn to several hospitals and a good deal of duplication occurs. It is not possible to estimate the populations at risk, and statistical studies of the E.M.S. hospital data must necessarily be made on the basis of proportionate morbidity. The usual method is to express the number of admissions for a defined disease or group of diseases as a proportion of the admissions for all causes within the same period of time, but this has two disadvantages. In the first place the incidence of injuries has no necessary connexion with that of illness and in the case of admissions from the Services may vary from time to time owing to factors' which have nothing to do with health. In the second place infective and respiratory illnesses have a regular and pronounced seasonal variation in frequency, not shared to anything like the same extent by other groups of illness. It follows that if as denominators of the proportionate morbidity rates we use the total admissions, the index for every other group of diseases is reduced to a considerable extent by the normal seasonal rise in infective and respiratory disease or by an unusual influx of injured patients. Real trends of illness are thus obscured and for this reason the proportionate morbidity indices I have used for the study of E.M.S. hospital statistics are based upon the total of non-infective and non-respiratory illness as denominator throughout.

It is possible at this stage to compare the statistics of the two halves of the year 1942, and the first half of 1943. In this paper I shall deal only with patients from the Services, divide the diagnoses into 12 major groups, and study (1) the sex differences, (2) the time trends for all men and all women as indicated by the three successive half-years and (3) the age-trend for men as shown by dividing them into four age-groups, under 25, 25-34, 35-44 and 45 upwards. The total numbers of illnesses and injuries coded, representing one-fifth of the admissions, were as follows for the successive half-years: Men, 20,815, 19,473, 17,461; Women, 1,707, 2,142, 2,546. The denominators of the half-year rates, that is to say the total numbers of non-infective and non-respiratory illnesses, were: Men, 12,757, 12,561, 10,579; Women, 1,089, 1,589, 1,784. The standard errors of a 10% rate, due to sampling and assuming no connexion between individual cases of the disease group would be, in the six groups: Men, 0·27. 0·27, 0·29; Women, 0·91, 0·75, 0·71. Fig. 3 shows the results of this analysis in. .ictorial form, uniform vertical scales of proportionate morbidity being used·th:·ot·.·t·out. Roughly, it may be said that the

ratio during that period was the prevalence of epidemic catarrhal illness in the year in question, the deaths of some tuberculous persons being thereby hastened, leaving fewer to die in the year following. The fluctuations in the influenza death-rate in each year are shown in the diagram for comparison. Here is an example of a disease for which notifications seems to have provided a rather more stable measure of incidence over a period of years than did the deaths.

Here I should like to interpolate a remark about the use of death-rates for specific diseases as a guide to their incidence. I am often told that we at the General Register Office place too much reliance on what doctors write on death certificates. My answer to that is that we are more interested in trends of death-rates with time, sex, age, locality, occupation, than with absolute measures of the rates, and unless there is reason to believe that doctors' mis-diagnoses and mis-statements are affected by one or more of these variables we are not greatly concerned. When the doctors play a biased game with their certification, as for example with coronary disease and social class, diphtheria and history of immunization, or where fashion in nomenclature changes rapidly, medical statistics may be seriously prejudiced. At the very beginning of life medical certification of cause of death is bad through insufficient means of diagnosis, but apart from that I do not think the wary statistician is being seriously misled by errors in death certification, and I am sure it will be a long time before certification of illness during life will approach to it in accuracy. There are too many reasons why the patient should not be allowed to know the whole truth, which no longer apply after death.

Returning to notification statistics, pneumonia is an example of a disease for which they provide a less satisfactory measure of morbidity than deaths. The rising ratio of notifications to deaths from 1921 to 1927 cannot have been due to a declining fatality, but was almost certainly explained by increasing completeness of notification in the early years after its inception. From 1928 to 1937 oscillations about a mean level of 1·5 occurred which corresponded inversely with pneumonia and influenza death-rates. Since we cannot suppose the fatality of the pneumonias to have been as high as two-thirds notification was still incomplete but nevertheless fatality rose in epidemic years, perhaps because it was higher for influenzal than for primary pneumonia. From 1940 the introduction of a more effective treatment for some forms of pneumonia was accompanied by a rise in the ratio to a new level of 1·9 in 1942. The increasing use of sulphonamide drugs at the first suspicion of onset of pneumonia will now probably cause a decline in notifications since the physician hesitates to notify if the classical symptoms fail to appear as a result of his early and heroic treatment. This growing tendency to apply powerful treatments on suspicion so that no diagnosis is ever reached in the successful cases is likely to cause headaches to medical statisticians in the future, but if the aggregate result is reflected in a declining total death-rate they can hardly complain.

These examples suffice to show that the morbidity measurer's millennium is not likely to be attained by making every disease notifiable. Such statistics tell us a good deal about the incidence of illness amongst children, but apart from tuberculosis and a few important but rare diseases they provide no index whatever of the total amount of illness in the adult population. Thus in the first two months of 1944 all notifications of illness amongst persons between the ages of 15 and 65 totalled about 14,000, but during the same period the number of persons of those ages who were laid up for at least one day on account of illness is estimated at about 8 millions.

HOSPITAL IN-PATIENT STATISTICS

The record papers of every patient admitted from the Army, R.A.F. and Women's Services to any hospital or portion of a hospital under control of the Emergency Medical Services organization are sent on his or her discharge or death to the registry of the Ministry of Pensions at Norcross, and in 1942 arrangements were made by which every fifth record should be examined there by a small staff of Ministry of Health coders and the main heads of information transferred to cards. The final diagnosis of the principal disease or injury for which the patient was admitted, the principal complication and principal acute and chronic subsidiary conditions unrelated to the primary, were to be coded by means of the M.R.C. Classification, then in process of compilation. Work began on the 1942 admissions in September of that year, and the records of 1942 have now been dealt with completely and those of the first half of 1943 provisionally. At the onset a choice had to be made between assembling the statistics according to date of admission or date of discharge. The former plan has the disadvantage that one must wait until the last patient has left hospital before tabulating the admissions during a given period. The alternative plan, which was used in the New York Hospital Discharge Study, is free from this difficulty but has the disadvantage that it does not give a true measure of incidence during the period under review. For example, many of the influenza patients admitted during December 1943 were not discharged until January and would appear in the statis-

tics of 1944. For this reason the former·plan·of working by date of admission was adopted notwithstanding the disadvantages entailed by time-lag. In practice the statistics are closed after a year has elapsed from the end of the period and provisional figures free from appreciable error can be tabulated at the end of nine months whilst approximate figures for some diseases can be obtained after shorter periods.

·This has made possible the study of the incidence curves of influenza and some related acute conditions during the recent epidemic shown in fig. 2. Three of the graphs show the estimated numbers of patients admitted from the Services to all E.M.S. hospitals during each week, from August to mid-January in the upper part of the diagram and to the end of February in the lower part, with a diagnosis of influenza (M.R.C. Nos. 070, 071, 073), coryza (No. 072) and acute sore throat (Nos. 481, 482). The fourth graph shows, on a scale at the right hand of the diagram arbitrarily chosen so as to bring the peaks to about the same height, the weekly influenza deaths in the great towns of England and Wales. The two parts of the diagram compare corresponding weeks in 1942-43 and 1943-44.

In the autumn and winter of 1942-43 when influenza deaths showed a normal seasonal trend, influenza admissions increased from about 50 per week in the autumn to about 240 per week in January. Milder catarrhs not described as influenza showed a corresponding January maximum, the weekly averages in successive months from August to February being about 5, 9, 12, 25, 35, 80, 45. Admissions for acute sore throat increased from about 120 per week in August to 210 in November-December and 200 in January, falling to 155 in February. In the autumn and winter of 1943-44 influenza admissions showed no excess over corresponding weeks of the previous year until the second week of October when the weekly number began to rise from about 40, reaching a peak of 875 in the last week of November. Deaths in the great towns increased at much the same rate with a time-lag of three weeks between the graphs. Admissions for milder catarrhs were also at a much higher level than a year earlier and they also reached their maximum in the last week of November. Acute sore throat admissions in successive months from August to December averaged about 150, 150, 160, 145, 100 per week, the incidence being apparently quite unaffected by the influenza epidemic, an interesting fact.

The card record system at Norcross has been so designed that if a patient is transferred from one E.M.S. hospital to another or to a convalescent depot, or is readmitted for the same complaint within a week of discharge, all the hospital records are brought together and count in the statistics as one illness only. This eliminates a defect which often mars aggregated civilian hospital statistics, since some patients are admitted in turn to several hospitals and a good deal of duplication occurs. It is not possible to estimate the populations at risk, and statistical studies of the E.M.S. hospital data must necessarily be made on the basis of proportionate morbidity. The usual method is to express the number of admissions for a defined disease or group of diseases as a proportion of the admissions for all causes within the same period of time, but this has two disadvantages. In the first place the incidence of injuries has no necessary connexion with that of illness and in the case of admissions from the Services may vary from time to time owing to factors which have nothing to do with health. In the second place infective and respiratory illnesses have a regular and pronounced seasonal variation in frequency, not shared to anything like the same extent by other groups of illness. It follows that if as denominators of the proportionate morbidity rates we use the total admissions, the index for every other group of diseases is reduced to a considerable extent by the normal seasonal rise in infective and respiratory disease or by an unusual influx of injured patients. Real trends of illness are thus obscured and for this reason the proportionate morbidity indices I have used for the study of E.M.S. hospital statistics are based upon the total of non-infective and non-respiratory illness as denominator throughout.

It is possible at this stage to compare the statistics of the two halves of the year 1942, and the first half of 1943. In this paper I shall deal only with patients from the Services, divide the diagnoses into 12 major groups, and study (1) the sex differences, (2) the time trends for all men and all women as indicated by the three successive half-years and (3) the age-trend for men as shown by dividing them into four age-groups, under 25, 25-34, 35-44 and 45 upwards. The total numbers of illnesses and injuries coded, representing one-fifth of the admissions, were as follows for the successive half-years: Men, 20,815, 19,473, 17,461; Women, 1,707, 2,142, 2,546. The denominators of the half-year rates, that is to say the total numbers of non-infective and non-respiratory illnesses, were: Men, 12,757, 12,561, 10,579; Women, 1,089, 1,589, 1,784. The standard errors of a 10% rate, due to sampling and assuming no connexion between individual cases of the disease group would be, in the six groups: Men, 0·27, 0·27, 0·29; Women, 0·91, 0·75, 0·71. Fig. 3 shows the results of this analysis in pictorial form, uniform vertical scales of proportionate morbidity being used throughout. Roughly, it may be said that the
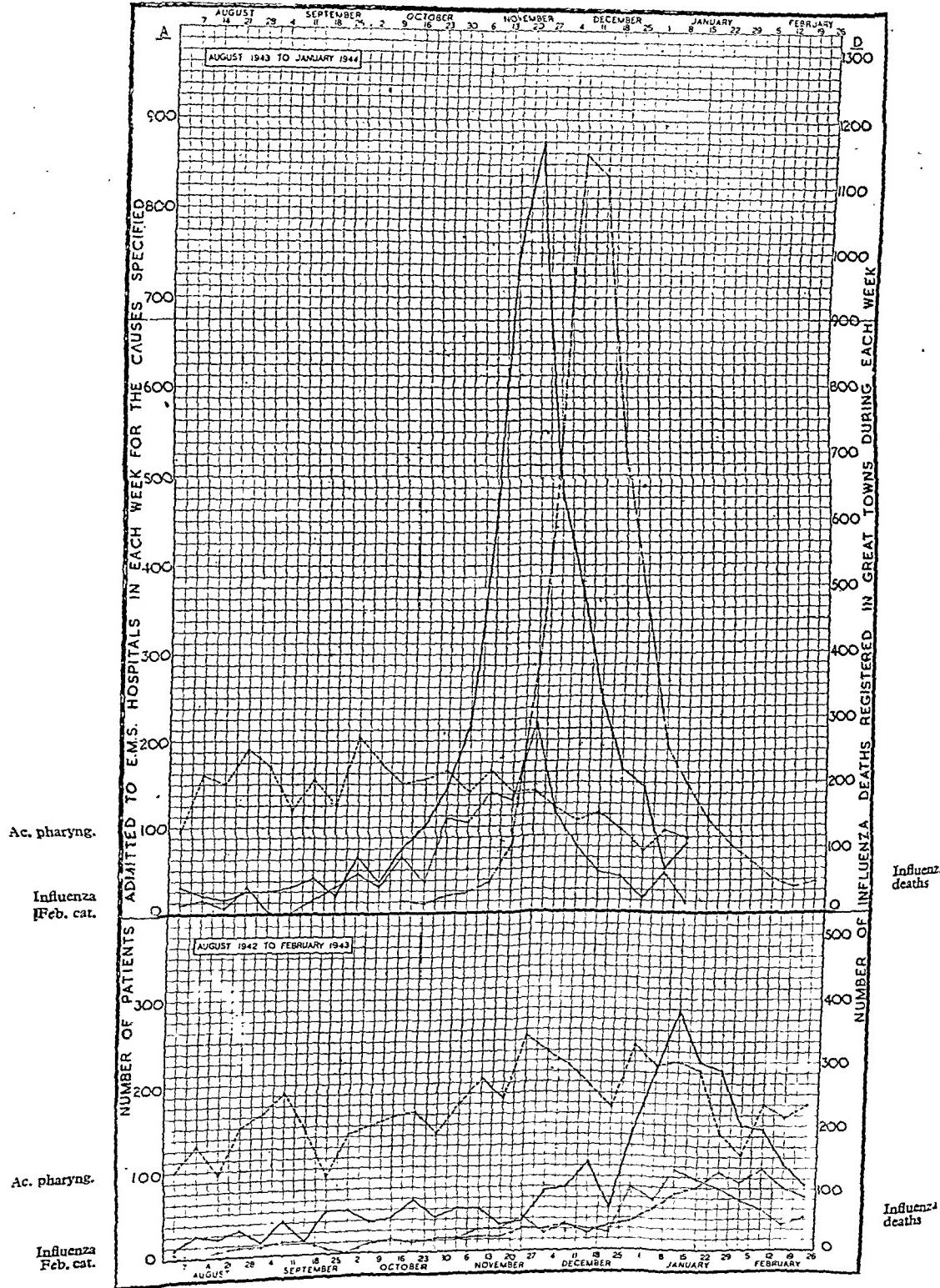
FIG. 2.—WEEKLY ADMISSIONS FROM THE SERVICES TO ALL E.M.S. HOSPITALS FOR INFLUENZA, COLDS AND ACUTE SORE THROAT.

Influenza (M.R.C. Nos. 070, 071, 073) ———
Febrile catarrh, colds (M.R.C. No. 072) — - - -
Acute pharyngitis, tonsillitis (M.R.C. Nos. 481-2) — - - -

Influenza deaths in)
great towns of } (D) — · —
England and Wales)

black columns (men) might be higher or lower by as much as one-twentieth of their height if every record had been coded instead of every fifth, and the shaded columns (women) might be higher or lower by as much as one-seventh. The ten broad groups of illness and two groups of injuries are based on the final diagnosis of the condition which caused the admission to hospital, and the *numbers after* the titles denote the Short List divisions comprising them. The Short List is a condensation of the M.R.C. Classification into forty-two headings thought to be most useful for general tabulations of morbidity statistics, and is shown in the Appendix with the M.R.C. code numbers making up each heading. The proportions per ·100 total non-infective and non-respiratory illnesses in the three half-years amongst the men and women patients are set out in Table I.

TABLE I.

Group (for Short List Nos. *see* Table II)	MEN 1942 1st	2nd	1943 1st	WOMEN 1942 1st	2nd	1943 1st
Infective disease	17·1	12·1	18·8	31·1	15·9	21·6
Respiratory disease ...	16·4	10·7	15·7	13·0	7·7	9·5
Mouth, throat, ear ...	10·9	9·9	8·2	14·4	12·1	12·7
Rheumatic diseases ...	5·3	4·9	5·3	5·1	5·5	5·3
Skin and eye affections	16·7	16·3	18·4	11·9	9·5	11·2
Bone and joint diseases ...	7·7	7·2	7·7	3·3	2·4	3·3
Nervous affections ...	12·0	12·2	12·3	9·2	9·7	9·2
Digestive diseases ...	15·8	16·9	15·1	20·0	23·1	20·4
Hernia	6·9	6·0	· 6·8	0·5	0·3	0·2
Circulatory diseases ...	9·5	9·6	8·9	2·6	3·1	4·9
Other defined illness ...	10·1	11·1	12·7	23·3	26·8	25·7
Ill-defined symptoms ...	5·1	5·9	4·6	9·7	7·5	7·1
Fractures, head injuries ...	14·0	15·0	14·6	5·1	4·5	4·9
Other injuries	15·7	17·2	16·1	7·5	6·8	6·7
Total illness and injury	163·2	155·0	165·2	156·7	134·9	142·7

Confining attention first to the secular trends and sex comparison, infective and respiratory diseases show in fig. 3 the expected excess in the first half of the year, lower indices for women in the first half of 1943 than a year earlier, female excess for infective diseases and male excess for respiratory disease in each period. Scabies accounted for much of the infective disease excess amongst women in 1942, their half-year indices being 9·1 and 3·9 compared with 1·3 and 1·0 for men; but in the first half of 1943 the scabies indices fell to 1·6 and 0·7 respectively. Tuberculosis also contributed 2·1 to the female excess in the first half of 1942 (4·8 compared with 2·7) but subsequently the rates for each sex were about 2½. Mouth, throat and ear affections showed a female excess due to acute pharyngitis and tonsillitis (No. 23) for which the indices were 10·5, 9·1 and 9·6 for women and 6·8, 6·5 and 4·8 for men; for ear and mastoid disease (No. 15) on the other hand the women's rates averaged 2·1 compared with 2·6 for men. The rheumatic group, made up of rheumatic fever and all forms of rheumatic arthritis and fibrositis, accounted for a uniform proportion of 5% in each sex. Skin and eye affections, excluding infestations of the skin, were more important causes of hospital admission amongst men, who also showed some increase in the first half of 1943, due to skin diseases. Bone and joint diseases likewise showed a male excess amounting to about 4½; and for hernia the men's indices were between 6 and 7 compared with less than ½ for women.

"Nervous affections" is a broad group covering organic nervous diseases (other than syphilis and intracranial vascular lesions), psychoneuroses and functional digestive disorders. No secular trend was evident, but the men's index was about 12 compared with about 9½ amongst women. For the group of psychoneuroses and abnormal character states (No. 11) alone the men's rates were 6·9, 7·0, 8·0 compared with 4·4, 5·5, 6·5 for women, each showing an upward trend, probably diagnostic rather than real. "Digestive diseases", excluding mouth and throat conditions, hernia, hepatitis, functional and symptomatic disorders, showed higher rates in the second half of the year for each sex, and pronounced excess amongst women. The female excess was due to appendicitis (No. 28), for which the women's indices (12·3, 13·1, 11·0) were three times as high as for men (4·1, 4·4, 4·2). For peptic ulcer, however, the men's rates (3·8, 3·6, 3·2) were about ten times as high as for women (0·5, 0·2, 0·4).

Circulatory diseases showed no secular trend amongst men but an excess over the women's rates, which was also apparent in the age-group under 25 (men 6·5, women 3·1). The large female excess for other defined illness was due to genito-urinary disorders (13·2 in 1942 compared with 4·0 for men) and to child-bearing. Ill-defined symptoms without an established diagnosis are recorded for about 4% of men and 6% of women admitted for any form of illness.

The relative importance of each of the 12 illness and injury groups at successive ages amongst men is indicated in Table II and fig. 3, the indices being percentage pro-
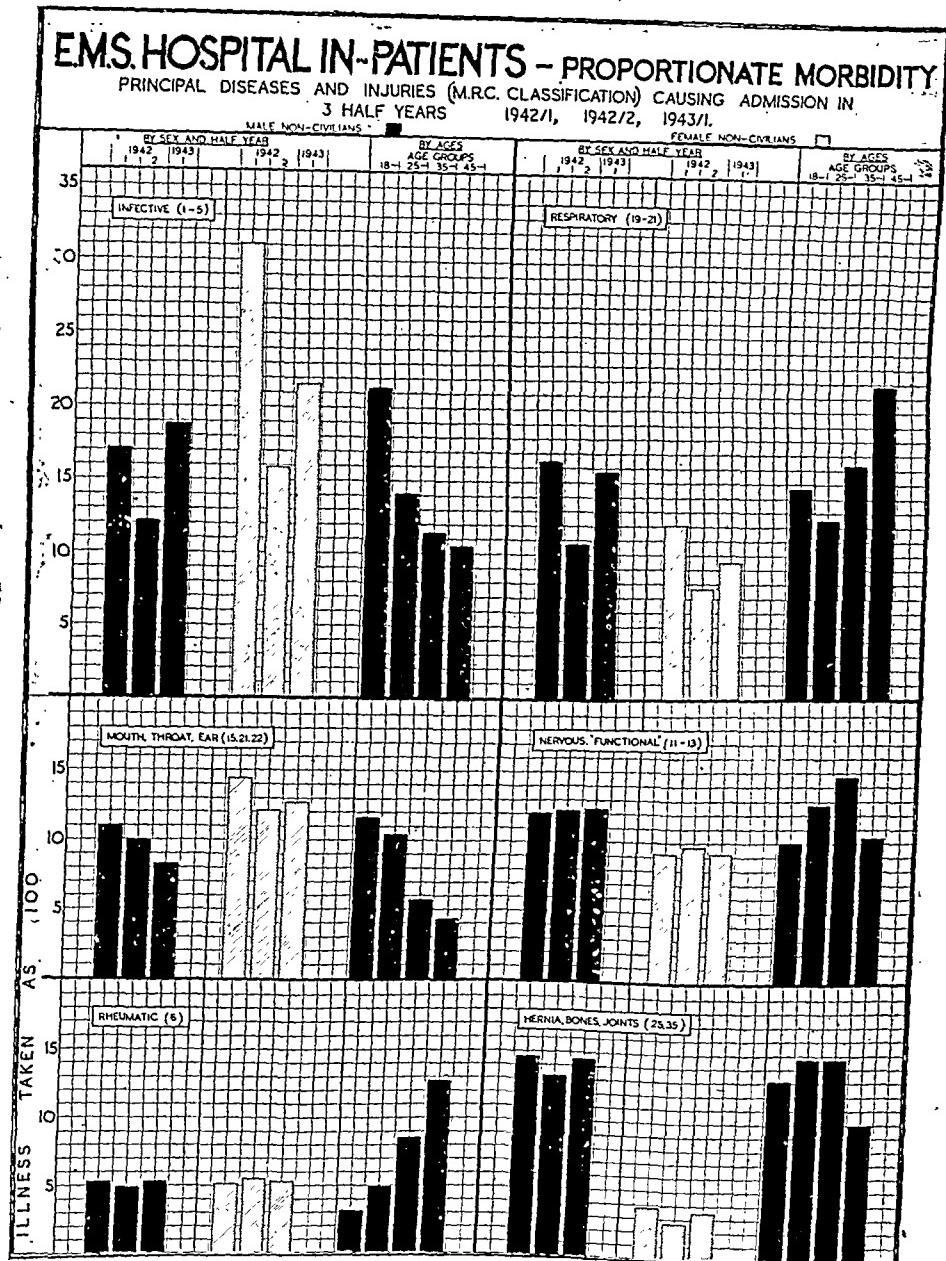
FIG. 3 (*continued on next page*).

portions of all non-infective and non-respiratory illnesses at the ages specified during the whole period January 1942 to June 1943.

Infective diseases, mouth, throat and ear diseases, skin and eye affections and injuries each showed a pronounced downward progression with advancing age. Rheumatic affections and circulatory diseases showed a pronounced upward progression as age increased, and this was true of respiratory diseases after 25-34. Nervous and "functional" affections were relatively most important at 35-44. Hernia was also maximal at that age, whilst bone and joint diseases became progressively less important after 25-34. Digestive diseases as a group showed no appreciable age-variation, nor did ill-defined symptoms, but the residue of other defined illness increased significantly after 45.
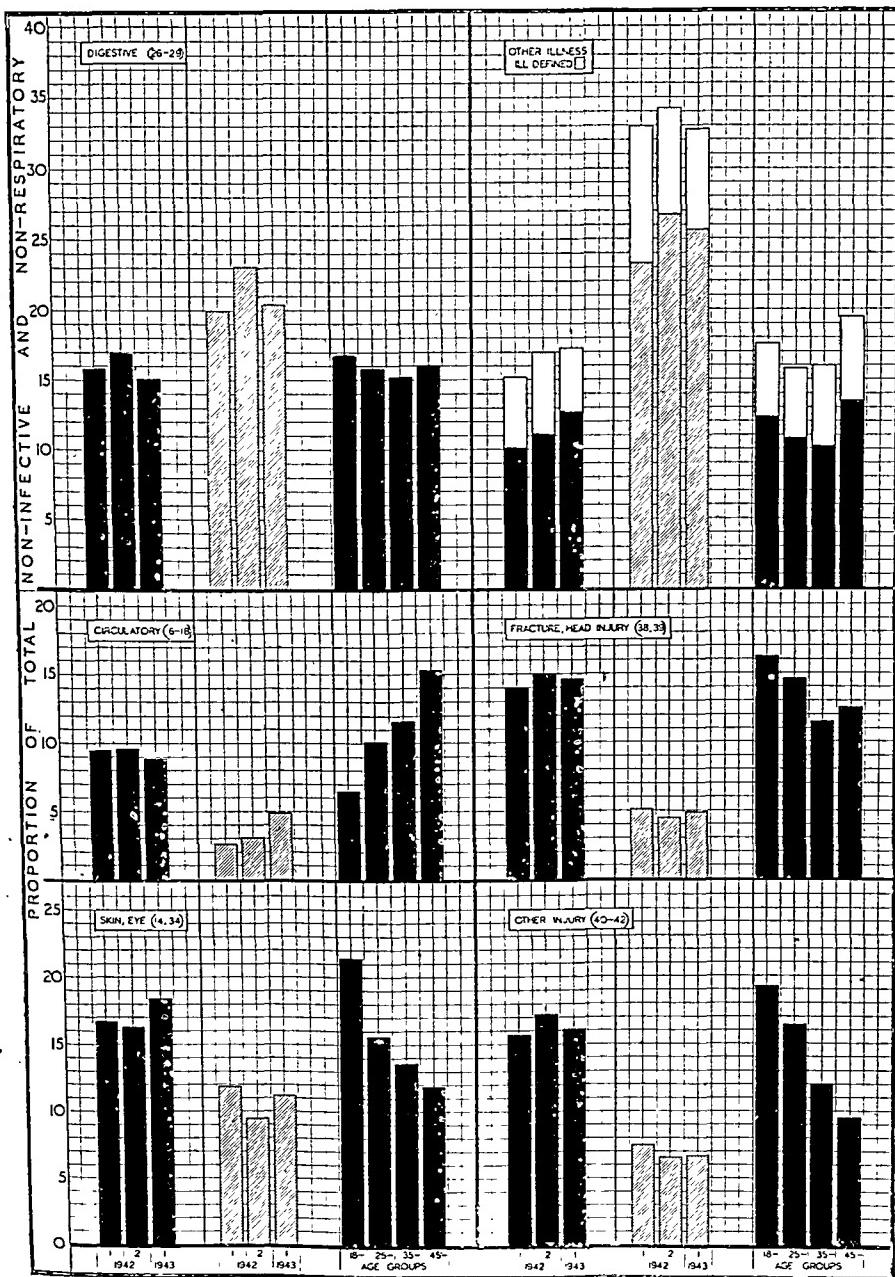
FIG. 3 (*continued from previous page*).

It is possible, of course, to standardize morbidity rates of any kind for the disturbing effects of varying age-distribution in the populations at risk, just as death-rates are standardized, and it is clear from the pronounced age-trends for some diseases in fig. 3 that this may be very necessary before drawing conclusions from comparisons between morbidity indices when the populations are selected as regards age. If a pronounced

TABLE II.

Short List Nos.	Group				MEN, BY AGE-GROUPS			
					18–24	25–34	35–44	45 and over
1–5	Infective disease ...	...	...	...	21·3	14·1	11·4	10·5
19–21	Respiratory disease	...	...	...	14·7	12·5	16·3	21·8
15, 22, 23	Mouth, throat, ear	...	...	...	11·6	10·4	5·7	4·3
6	Rheumatic diseases	...	...	...	3·1	4·9	8·5	12·7
14, 34	Skin and eye affections	...	...	...	21·4	15·6	13·6	11·9
35	Bone and joint diseases	...	...	...	6·7	8·4	7·1	4·5
11–13	Nervous affections	...	...	...	10·0	12·7	14·7	10·4
26–29	Digestive diseases	...	...	...	16·7	15·8 ·	15·2	16·0 ·
25	Hernia	...	...	...	6·4	6·3	7·6	5·4
16–18	Circulatory diseases	...	...	...	6·5	10·1	11·6	15·3 ·
7–10, 24, 30–33, 36 }	Other defined illness	...	...	...	12·3	10·8	10·2	13·5
37	Ill-defined symptoms	..	...	...	5·3	5·0	5·8	6·0
38, 39	Fractures, head injuries ...	...	· ...,		16·2	14·6	11·5	12·5
40–42	Other injuries ...	...	...	...	19·2,	16·4	12·0	9·5
1–42	· Total illness and injury				171·4	157·6	151·2 ·	154·3

change in age constitution of the E.M.S. hospital patients occurred between the first half of 1942 and a year later, the comparison between the three half-years might be invalid for some of the disease groups. In order to test this we may take as an example mouth, throat and ear affections which showed amongst men a pronounced downward trend with advancing age when the three periods were combined and an apparent fall from 1942 to 1943 when all ages were combined. Could the latter be explained by a changing age constitution of the hospital population? If the age-specific proportions in Table II are applied to the numbers of men admitted for all non-infective and non-respiratory diseases at the corresponding ages in the three half-years separately, the numbers of men of all ages with mouth, throat and ear affections would have been 1,253, 1,230, 1,022, and expressing these as percentages of the total numbers with non-infective and non-respiratory diseases at all ages, the standard morbidity indices would be 9·8, 9·8 and 9·7. These show no appreciable downward trend and consequently changes in age-constitution did not account for the observed trend of the crude rates, viz. 10·9, 9·9, 8·2. The three standard indices differed so little that standardization is evidently not necessary when comparing any of the morbidity indices in the three half-years. There is no doubt that standardization would affect the comparison between the men's and women's indices for diseases showing pronounced age-gradients, since the women were more concentrated into the age-group under 25. This is one of the refinements of morbidity statistics which we shall have to keep in mind.

The E.M.S. hospital statistics, relating as they do to men and women in the Services distributed over the whole country, provide a tolerably good measure of all illness considered by Service standards to be severe enough to require hospitalization. The only factor which may have operated selectively was the choice between a military hospital and an E.M.S. hospital in a few areas where both were available or for conditions such as psychoneuroses with special E.M.S. treatment centres. There is no reason to suppose that this had appreciable influence on the time-trends or the sex and age comparisons, though certain diseases and injuries may have been under or over-represented in the E.M.S. patients in consequence. The standard of what constituted illness would be reasonably low and constant, though not comparable with any civilian standard. In the civilian population these criteria are not fulfilled and civilian hospital in-patients statistics alone can tell us little about the total incidence of illness, since they are highly selective in many different respects.

TOTAL MORBIDITY IN THE GENERAL POPULATION

Morbidity in the general population might be measured by means of hospital in-patient records, combined with complete records of attendances at out-patient departments, clinics and doctors' surgeries and of domiciliary visits by doctors. The assembly of data from these various sources of information is fraught with difficulties, but an interesting experiment on these lines is now being made by the Bureau of Sickness Records at Oxford, of which Professor Ryle has given some account. Under his direction this will provide in the course of time useful data about the medical treatment received by residents in that area for different kinds of illness and injury.

Another method of approaching the problem is by means of the medical certificates required for claims of sickness benefit from the National Health Insurance fund, but these cover only the insured population and illnesses incapacitating for four days or more. They are also affected, perhaps considerably, by changing attitudes to the relative importance of keeping at work and of safeguarding the health of the persons affected and of others. These attitudes are, in their turn, influenced by economic conditions, amount of unemployment, wage-rates, benefit-rates, health propaganda and education, and the up-

ward trend of sickness claims both in this country and America in the period between the trade depression and the onset of the war was probably due to these factors rather than to increase in the amount of illness. The war introduced other disturbing factors such as increased hours of work and reduced holidays leading to fatigue, the natural effect of which would be to lengthen the period before returning to work in many cases and to increase the numbers making claims for slight degrees of illness. To some, slight illness, which in normal times would have been thought little of, has offered the only chance to obtain a much-needed rest; to others the longer working hours to be faced on return may have been a deterrent from going back too quickly. For these reasons National Insurance statistics do not provide a reliable measure of the trends of absolute incidence of illness, though when analysed by causes of incapacity as in the Scottish reports of pre-war years they give useful information about the trends of proportionate morbidity.

Another method, applicable to industrial workers, including the Civil Service, is to analyse the records of certificated absence from work, using the doctor's certificate to the employer for the purpose of diagnosis classification. The reports on illness in the Canadian Civil Service provide an example; and the Industrial Health Research Board in this country is about to employ this method in factories, using a condensed grouping of illnesses based on the M.R.C. Classification and the Short List to which I have already referred.

These methods have the advantage that the diagnosis is written down on some certificate or record by a doctor, but since the patient usually sees the certificate and is just commencing treatment, and since recovery is likely to be much influenced by what the patient is told, we cannot assume that these certificates contain the whole of what was in the doctor's mind. Indeed it is doubtful whether diagnoses based on such certificates at the onset of illness are on the whole as reliable as information given by the patient *after the illness is over* as to what the doctor told him or her about its nature.

The experimental survey of sickness incidence in the civilian population which was carried out during last winter by the Wartime Social Survey on behalf of the Ministry of Health, employed the last-mentioned method on a sampling basis. The advantages were that it covered the whole civilian population between ages 16 and 65, whether industrial or insured or neither, and that the questions related to all illness and injuries experienced during three months, whether a doctor was consulted or not, supplemented by details of the time laid up in bed and lost from work, medical attendance and social conditions. The districts to be visited were first chosen, distributed in proper proportion according to region, large and small towns and rural districts, the correct quota was allotted to each and the individuals to be interviewed were chosen by a random process from the local food card registers. A Field Worker of the Wartime Social Survey then visited each address and completed a schedule for the person concerned. If he or she could not be seen, nor a reliable informant, a substitute individual, also selected at random, was visited, this being necessary for about 14%. Different samples of about 2,500 people from different areas were thus interviewed at the beginning of each month, January, February and March, the period of experience being the three months preceding the interview and thus overlapping. The month in which each illness began was recorded and consequently incidence rates in November and January were ascertained from two, and in December from three, entirely independent samples, thus providing a useful check on the assumption that each sample was representative of the population as a whole.

Every illness recorded was coded according to the M.R.C. Classification by coders experienced in this work, and was then assigned to its appropriate category of severity. These categories were defined as follows—*Serious*: Usually producing total incapacity to work for four weeks or more, or involving considerable risk of death (immediate or delayed). *Moderate or mild*: Usually producing total incapacity to work for three days or more, but not serious as defined above. *Minor*: Ailments of defined diagnosis which usually do not incapacitate from work for as long as three days at a time. *Symptomatic*: Symptoms without definite diagnosis (No. 76 in M.R.C. Code). Diseases of very variable effect on capacity for work were left in an indeterminate group and for these the number of days of incapacity which actually occurred was used to fix the category, influenza being dealt with in this way owing to the fact that a self-diagnosis of "flu" was often made although the person affected had not been away from work, or away for only one or two days. A provisional allocation of the M.R.C. code numbers to these categories was made in consultation with Professor Ryle and Dr. J. A. Glover. Colds were classed in the Minor group. In addition to this grouping by severity, illnesses were also assembled into the Short List groups and according to the number of days lost from work, or laid up in bed in the case of workers at home, and information was obtained about chronic or recurring illness which started before the three-month period.

The results of this experiment have been reported on as regards the monthly incidence

of illness in the Monthly Bulletins of the Ministry of Health and E.M.S. Laboratory Service for April, May and June 1944, and the correlation with social factors will be dealt with in a report by the Wartime Social Survey. Here I can only briefly compare the monthly incidence rates of each category of illness and of influenza and colds according to the three successive samples. Fig. 4 reveals both the strong and weak points in this method of morbidity measurement. For the serious and moderate or mild categories of illness the agreement between the samples, as indicated by the heights of the overlapping columns, was well within the range of error to be expected from the size of the samples, and the experiment has demonstrated that the combination of three samples of 2,500 each will give sufficiently reliable monthly rates of incidence of these grades of illness in the population as a whole. This was true also of the group of ill-defined symptoms such as headaches and coughs. For the group of Minor ailments, in persons who had nothing worse to record during the month, the agreement between the samples was not so good, and for the months of November and December when influenza was epidemic the incidence recorded at interviews early in February was only about three-quarters of that recorded for the same month at interviews early in January. The third sample, interviewed early in March, showed a further slight deficiency for December and a slight excess for January. During the epidemic, colds and attacks described as influenza or "flu" which incapacitated for less than three days formed a large part of the Minor ailment group, and in fig. 4 the same discrepancies in the November-December rates are apparent for this group of complaints considered independently of any other illness. This falling off in the minor ailments recorded after a lapse of time might well be explained by the short memory we have for trivial ailments such as colds, but the fact that no such effect appeared for January suggests that it may have been due rather to a tendency to exaggerate symptoms into actual attacks whilst the influenza epidemic was still very much in people's minds at the beginning of January, whereas that tendency had subsided a month later, when the epidemic was known to be over. At the foot of the diagram the downward progression of the columns is still evident after eliminating the attacks which did not incapacitate for as much as a day and, strange to say, it was more pronounced amongst men than women. More experience must be awaited before we can see whether memory will prove to be important in non-epidemic periods. In the meantime we may attribute part of the epidemic discrepancies to memory and part to exaggeration and simply combine the samples in order to obtain the monthly minor ailment rates. The resulting monthly incidence of the four categories of illness (selecting the highest category if more than one illness started in a month), per 1,000 persons, is shown in Table III.

TABLE III.

Illness category	October	November	December	January	February
Serious	17	19	20	19	21
Moderate or mild	78	117	152	139	156
Minor	126	172	246	229	264
Symptomatic	34	36	37	45	53

The sum of the four rates gives the proportion of people who experienced some departure from health important enough for them to remember and mention some months later. For the five successive months October to February the percentages were 24½, 34½, 45½, 43 and 49½; ignoring minor and symptomatic ailments they were 9·5, 13·6, 17·2, 15·8 and 17·7. Each of these measures indicated an increasing incidence of illness from October to December, a slight fall in January and then a further rise in February to a level rather above that of December. If, however, we take into account the duration of incapacity the trend was rather different, for within each category a pronounced shortening of the average duration occurred in January and a further slight shortening in February. Consequently the average duration of incapacity caused by all categories of illness per head of the population aged 16 to 65 was about 2·1 days in November, 2·0 in December, 1·4 in January and 1·3 days in February. During the three months November to January the average number of days laid up per head of the population was about five and a half, to which serious illnesses contributed about two, moderate and mild illness three days and minor and symptomatic ailments about half a day. Some further experience from overlapping periods will be needed before deciding which is the best index of morbidity to use for those who like to have their statistics in tabloid form.

With regard to the incidence of separate forms of illness during the five-month period, the monthly rates per 1,000 of each sex for influenza, colds and laryngitis (Short List No. 3) causing incapacity for at least one day were as follows:—

	October	November	December	January	February
Males	31	80	106	63	55
Females	30	70	102	59	35

Incidence increased from about 3% after in October to over 10% in December and by February had almost regained the Oct er level. For some other common complaints
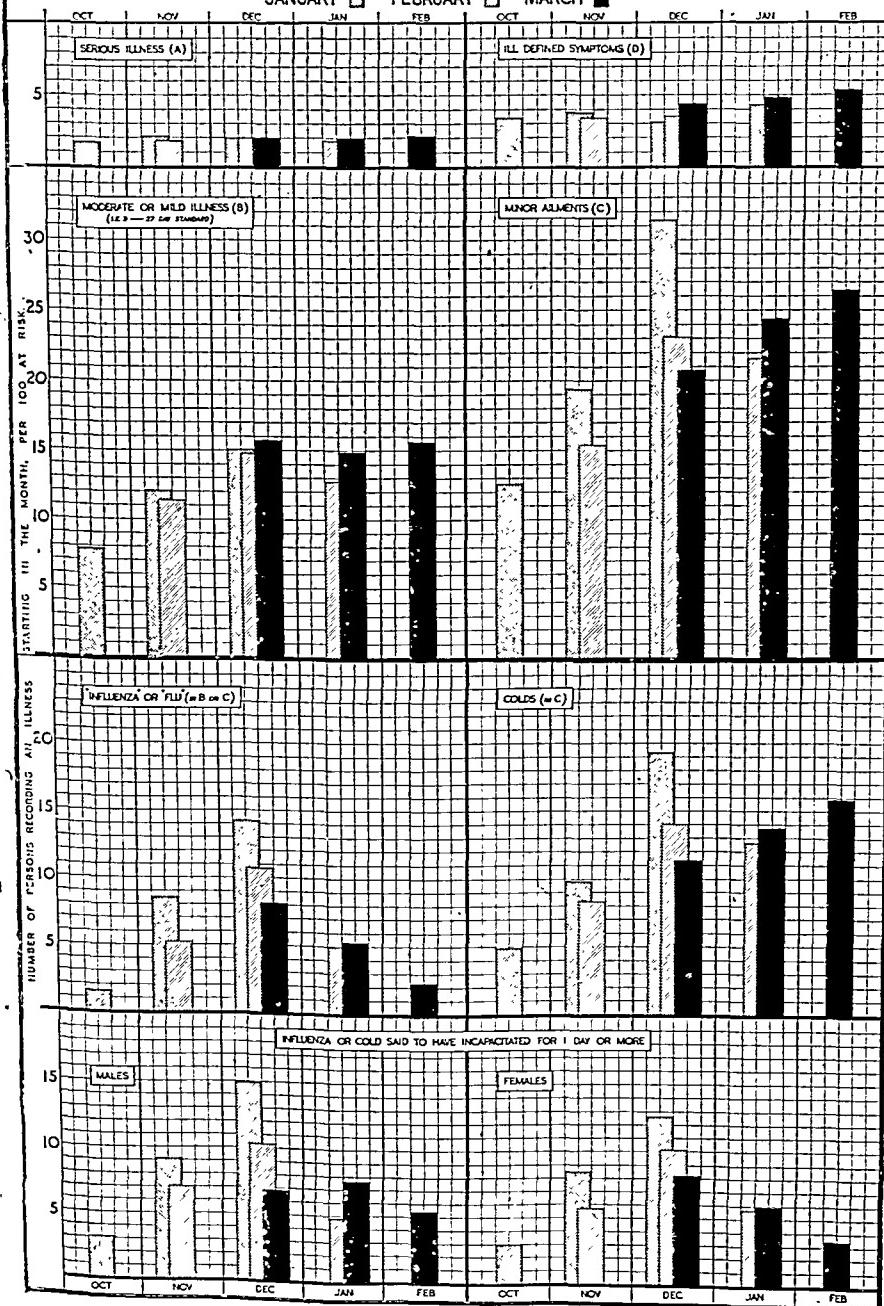
FIG. 4.

rates of incidence during three months, per 1,000 persons and based on a total of 6,745 at risk, are given below:

M.R.C. Code							Rate
706	Muscular rheumatism...	...	...	...	...	...	49
7609	Headaches ...	...	...	...	...	...	32
4903, 5113	Gastritis and dyspepsia	...	...	...	...	...	23
481, 482	Acute sore throat	...	...	...	...	...	16
3620	Blepharitis ...	...	...	...	...	...	10
4270	Chilblains ...	...	...	...	...	...	9
211	Asthma ...	...	...	...	...	...	8
325	Neuralgia and neuritis	...	...	...	...	...	8
430, 434	Varicose veins and phlebitis (legs)	...	...	...	...	7
2747	Anæmia...	...	...	...	...	...	7
323	Sciatica	...	...	...	...	...	5
6807	Boils ...	...	...	...	...	...	3
431	Hæmorrhoids ...	...	...	...	...	...	3
4541	Pleurisy ...	...	...	...	...	...	3
452	Pneumonia · ...	...	...	...	...	...	2
096	Scabies ...	...	...	...	...	...	2
0780	Herpes zoster ...	...	...	...	...	...	1·5

The method of domiciliary visitation and compilation of health histories from individuals and families has been employed to good effect in America, usually by household sampling in a selected town. The famous Hagerstown study reported on by Collins as long ago as 1929 proved the usefulness of the method and was followed by many others. In this country we were slow to experiment on these lines, but it is clear, I think, that this instrument can be used not only for studies of special medical problems as they arise but also for collecting much-needed information in the wide fields of social medicine. The monthly survey will be resumed in July and it is hoped to be able to deal also with other age-groups so that eventually we shall obtain a continuous measure of morbidity in most sections of the population.

INDIVIDUAL HEALTH HISTORIES

There are other sources of information for the measurement of morbidity amongst children, namely the records of infant welfare and school medical departments. Hitherto the period between infancy and admission to school during which the foundations of ill-health are often laid has been, except for notifiable diseases and deaths, almost uncharted and it is to be hoped that this will be remedied by the new Education Act. The statistical work of Derrick, McKinlay and others on generation mortality suggests that the changes in the average environment to which children born in successive periods of time are exposed in their early years tend to impress themselves on subsequent rates of dying throughout life. The Registrar-General has called attention to progressive movements of the age of maximal death-rate from cancer and some other chronic diseases, and such changes in the age-mortality curve may reflect not what is happening to the disease now but what happened several decades ago when the pathological process was commencing. The conquest of acute diseases is likely to continue with increasing rapidity and consequently chronic degenerative diseases will assume a greater importance in the general morbidity picture. It is improbable that such conditions will respond greatly to chemotherapy; it is more likely that we shall have to go back to their beginnings and try to remove or counteract the irritant causes which, when unchecked, eventually produce them. Before we can identify these causes it may be necessary to study by statistical methods the continuous health histories of very large numbers of individuals of all occupations and classes, and in this the methods of morbidity recording I have mentioned will not help us. Cross sections of the population alone, no matter how complete and how frequent, can give no complete answers to these problems of chronic disease. They need to be supplemented by individual health histories extending over long periods of time.

The Oxford Bureau envisages this, but at present that part of their plan is an act of faith, for it is handicapped by considerable gaps in the medical histories obtainable under present arrangements, and also by the necessary limitation to those people who are born within and continue to live within the area of the survey. Social medicine will at every turn be restricted by these limitations, and if we are really interested in its development we shall have to try to remove them. The ultimate aim is to keep for every individual a record of every event of health significance from the time of conception to death, and to establish a system by means of which a person does not cease to exist statistically when he removes to another administrative area. The building up on a national scale of individual health histories is no new idea—it has been in our minds at the General Register Office since the time of Farr. Not until now, however, have we had the administrative machinery for it ready at hand and a public opinion educated to the point of being ready to welcome it. In my opinion it should be started forthwith for every newborn child, with, as first object, the keeping of continuous records of every event directly or indirectly affecting the child's health up to the age of 15. We may

anticipate that before the children now being born have reached that age a National Health Service will have been developed which could continue to take care of their records throughout life.

The immediate plan might be formulated somewhat as follows. At the time when an expectant mother draws the food ration book for her child she could be given also a health book consisting of a series of detachable slips and counterfoils. The first slip could be devoted to any prenatal events, and the second to any natal events of significance, and could be filled in by the doctor or nurse in attendance. On registering the birth the first two slips could be detached and sent to the central office marked with the child's national registration number, which would also be impressed on all the remaining slips in the book (or in the case of a still-birth the book could be retained and sent to the central office). On the statistical record of birth registration the national registration numbers, both of child and mother, could be entered so that all the details ascertained at birth could be brought into relation centrally, for statistical purposes only, with the subsequent health history of the child as told by the slips as they come in. Special slips in the health book could be devoted to vaccination, immunization against diphtheria, other inoculations and school admission, and the remaining slips to illnesses or injuries attended by a doctor. During the first year of operation of the plan a doctor attending any child under one year of age would ask for the health book, the used counterfoils of which would tell him the child's previous record. During the second year this would be extended to all children under two years of age and so on. On first seeing the child for an illness or injury he would write a provisional diagnosis on the next slip and counterfoil, and the date, and the doctor who finally discharged the child would add the final diagnosis, and by some arrangement the slip would then be detached and sent to the central office. In this way the counterfoils of the health book in the care of the child's parent or guardian would contain a continuous health history, whilst the slips reaching the central office could, by means of the national registration number, be assembled to produce individual and family health histories for statistical purposes. On registration of death of a child in possession of a health book the national registration number would be entered on the statistical record of death registration.

Amongst the gaps in our knowledge which might thus be filled within a few years of starting the plan are—the medical causes of stillbirth and its differential incidence according to occupation and social class concerning which we have no adequate information in this country; the prenatal maternal conditions associated with premature birth and neonatal morbidity and mortality; the subsequent health histories and survival rates of prematurely born children as compared with full-time children; morbidity of children according to size of family, spacing of births and social class of parents; immediate fatality of certain diseases of children; efficacy of immunization against certain diseases as measured by incidence of the disease in successive years after it has been done. These problems are much in the minds of biologists, obstetricians, pædiatricians and social reformers, some of whom criticize the statisticians because they cannot be answered. No responsible statistician ought to advocate the starting of an expensive investigation merely because the facts brought to light are likely to be "interesting". At the stage of medical and social progress we have now reached these questions seem to me to be not merely interesting but vital if the study of social medicine is to result in anything better than a lot of pious platitudes. What I have suggested would not be dependent upon a census, and in its early years it would make small demands upon the doctors. Indeed, the saving of time through having a child's history in concise form written on the counterfoils of the health book might, I believe, exceed the time expended in writing down a diagnosis. It would rapidly provide a national and unselected body of information from which samples could be taken to answer specific questions about birth and infancy. Eventually it would provide a statistical framework linking the maternity, pædiatric and school medical services to one another and to adult health services, which are at present sadly disconnected.

"The thing to aim at ultimately is a Return of the cases of sickness in the civil population as complete as is now procured from the army in England. It will be an invaluable contribution to therapeutics as well as to hygiene; for it will enable the therapeutist to determine the *duration* and the *fatality* of all forms of disease under the several existing systems of treatment in the various sanitary and social conditions of the people. Illusions will be dispelled; quackery as completely as astrology suppressed; a science of therapeutics created; suffering diminished; life shielded from many dangers. The national returns of cases, and of causes of death will be an arsenal which the genius of English Healers cannot fail to turn to account." ·

This passage from the Supplement to the 35th Annual Report of the Registrar-General (p. lxxx) was written by William Farr in 1874. I wonder whether he expected that

seventy years later one of his successors would be suggesting, in halting and apologetic language, that a beginning should at last be made to achieve this aim.

APPENDIX

SHORT LIST OF DISEASES AND INJURIES BASED ON THE MEDICAL RESEARCH COUNCIL'S CLASSIFICATION, 1944

Group No.	Title of group	M.R.C. Code Nos.
1	Tuberculosis...	02, 03
2	Venereal diseases and sequelæ	04, 05
3	Colds, influenza and laryngitis	070-073, 443
4	Scabies	096
5	Other infective diseases	Rest of 00-09
6	Rheumatism, arthritis, fibrositis	10, 700-706
7	Neoplasms	11-20
8	Diabetes	22
9	Anæmias	270-274
10	Other general and endocrine diseases	Rest of 21-29
11	Psychoneuroses and abnormal character states	331-333
12	Functional disorders of digestion ...	51
13	Other diseases of nervous system (excluding intracranial vascular lesions)	30, 32, 330, 34, 35
14	Diseases of eye and visual defects...	36
15	Diseases of ear and mastoid	37
16	Intracranial vascular lesions	31
17	Diseases of heart and arteries	38-42
18	Disorders of veins ...	43
19	Pneumonia (acute primary)	450-452
20	Bronchitis (including tracheitis)	445-448
21	Other diseases of respiratory system	Rest of 44-46
22	Diseases of mouth and teeth	47
23	Acute pharyngitis and tonsillitis	481, 482
24	Acute hepatitis and jaundice	540, 541, 543, 7686
25	Hernia	520-525
26	Gastric and duodenal ulcer	491-494
27	Gastro-enteritis	500-503
28	Appendicitis	507
29	Other diseases of digestive system	Rest of 48-50, 52-55
30	Diseases of female genital organs ...	60, 61
31	Other genito-urinary diseases (non-venereal, including nephritis)	56-59
32	Normal child-bearing	620, 650
33	Abnormal child-bearing	Rest of 62-67
34	Diseases of skin and cellular tissue	68, 69
35	Diseases of bones, joints, muscles (non-rheumatic)	71, 72
36	Congenital malformations and infantile diseases	73-75
37	Ill-defined symptoms (except jaundice)	76 (except 7686)
38	Head injuries	800, 840
39	Fractures (except of skull)	841-845
40	Acute poisoning	90-92
41	Burns	93
42	Other injuries	Rest of 80-96

Mr. L. Moss (Wartime Social Survey) said that the fact that with moderate illness there was some discrepancy between the number of people saying they had suffered from one sample to another, indicated that such factors as memory were likely to be important in getting an accurate picture. One way to deal with this would be to shorten the lapse of time between the interview and the period to which the questions asked, apply. Thus, it might be that reducing the lapse of time to a maximum of two months from the incidence of illness would considerably reduce the discrepancy shown on Dr. Stocks's chart.

Early sampling data showed that the sampling technique itself proved very efficient and that the discrepancy between figures on different dates could not be put down to this, or to the fact that different investigators were at work. The same team of investigators had been engaged on each inquiry.

Dr. V. Freeman (Islington): The measurement of morbidity would be greatly favoured by the establishment of Health Centres under the White Paper proposals since statistical and clerical staff could be made available to the doctors to assist in the proper recording of the work done on a statistically sound basis. At least one of the staff at the Health Centre should therefore be a trained worker, responsible for the medical records and vital statistical tabulation of the work done at the Centre. The attention of the Minister of Health should be drawn to the importance of this aspect and allowance made for the necessary staff when planning the Health Centres.

Dr. Avery Jones (Middlesex) hoped that the new M.R.C. Classification of Diseases would be widely used in hospitals. An adequate classification of diseases was the first essential for clinical research and enabled previous case records to be re-examined. In many hospitals the existing classifications were totally inadequate and much clinical material was lost unless private records were kept. The M.R.C. System had been in use for six months at the Central Middlesex County Hospital where there was an in-patient turnover of 11,000 cases a year and could be applied by clerical staff with a minimum of medical supervision. It had, therefore, a great advantage over the American Logie System.

Section of Urology

President—E. W. RICHES, M.C., M.S.

[*April 27, 1944*]

Dissolution of Urinary Calculi

By Captain HOWARD I. SUBY, U.S.A.M.C.

(*From the Dept. of Urology, Massachusetts General Hospital, Boston, Mass., U.S.A.*)

THERE are six common chemical types of urinary calculi: (1) Calcium phosphate; (2) calcium carbonate; (3) magnesium ammonium phosphate; (4) calcium oxalate; (5) uric acid; (6) cystine. It is with only the first three, calcium phosphate, calcium carbonate, and magnesium ammonium phosphate, that this paper is concerned. In a previous communication the possibility of using an isotonic citrate solution at a pH of 4·0 to dissolve urinary calculi was discussed (Albright *et al.*, 1939). This solution was a good solvent of calcium phosphate and was used successfully on a case of bladder stones in a patient with a "cord bladder". Since his sensory mechanism was diseased, this patient complained of no irritation, but subsequently developed a suppurative cystitis and epididymitis. It was apparent that this solution was far too irritating for routine clinical use. In collaboration with Dr. Fuller Albright studies were therefore undertaken to determine both the solvent properties and the irritations of various organic acids in varying concentrations and pH levels. The speed with which these solutions would dissolve calcium phosphate calculi was determined by the speed with which they decalcified rabbits' teeth. Approximately 80 solutions were tested. Concomitantly, studies were started to determine the irritability of these solutions to living tissues. Obtaining an efficient solvent which was not too irritating to the tissues of the urinary tract was the big problem. Experiments which allowed test solutions to drip over the conjunctivæ of anæsthetized rabbits were first done. These gave a rough idea of the irritability of solutions but were not accurate enough to make fine distinctions. The lighter the anæsthesia, the more the rabbit would blink, and the more irritated would the conjunctiva become. Test solutions were then used for intermittent bladder irrigations in anæsthetized female dogs. After a period of two, or three hours' irrigation with the test solution, the dog was cystoscoped and the condition of the bladder mucosa ascertained. This method was impracticable because of the large number of solutions which required testing. Finally a method using a two-way catheter in the bladder of anæsthetized female rabbits was used which proved very satisfactory. Solution was run into the inlet tube of the two-way catheter at a rate of about 120 drops per minute, and would flow out the outlet tube of the two-way catheter. This process was continued four hours. The appearance of the outflow solution was noted, and the time and amount of bleeding, if any, was recorded. At the end of the four-hour period, the rabbit was autopsied and the bladder mucosa studied grossly and microscopically. Controls using normal saline were done, and these showed no change in the gross or microscopic appearance of the bladder wall. Many organic acids with variations of tonicity, pH, and temperature were then used as test solutions. The irritability seemed to depend upon: (1) Tonicity; (2) pH; (3) specific chemical factor.

Solutions with a pH below 4 so far have proved impracticable as they produce too much bleeding and œdema. After many experiments it seemed that the most practicable solution from the point of view of solubility and irritability was an isotonic solution of

seventy years later one of his successors would be suggesting, in halting and apologetic language, that a beginning should at last be made to achieve this aim.

APPENDIX

SHORT LIST OF DISEASES AND INJURIES BASED ON THE MEDICAL RESEARCH COUNCIL'S CLASSIFICATION, 1944

Group No.	Title of group	M.R.C. Code Nos.
1	Tuberculosis...	02, 03
2	Venereal diseases and sequelæ	04, 05
3	Colds, influenza and laryngitis	070-073, 443
4	Scabies	096
5	Other infective diseases	Rest of 00-09
6	Rheumatism, arthritis, fibrositis	10, 700-706
7	Neoplasms	11-20
8	Diabetes	22
9	Anæmias	270-274
10	Other general and endocrine diseases	Rest of 21-29
11	Psychoneuroses and abnormal character states	331-333
12	Functional disorders of digestion ...	51
13	Other diseases of nervous system (excluding intracranial vascular lesions)	30, 32, 330, 34, 35
14	Diseases of eye and visual defects...	36
15	Diseases of ear and mastoid	37
16	Intracranial vascular lesions	31
17	Diseases of heart and arteries	38-42
18	Disorders of veins	43
19	Pneumonia (acute primary)	450-452
20	Bronchitis (including tracheitis)	445-448
21	Other diseases of respiratory system	Rest of 44-46
22	Diseases of mouth and teeth	47
23	Acute pharyngitis and tonsillitis	481, 482
24	Acute hepatitis and jaundice	540, 541, 543, 7686
25	Hernia	520-523
26	Gastric and duodenal ulcer	491-494
27	Gastro-enteritis	500-503
28	Appendicitis	507
29	Other diseases of digestive system	Rest of 48-50, 52-55
30	Diseases of female genital organs ...	60, 61
31	Other genito-urinary diseases (non-venereal, including nephritis)	56-59
32	Normal child-bearing	620, 650
33	Abnormal child-bearing	Rest of 62-67
34	Diseases of skin and cellular tissue	68, 69
35	Diseases of bones, joints, muscles (non-rheumatic)	71, 72
36	Congenital malformations and infantile diseases	73-75
37	Ill-defined symptoms (except jaundice)	76 (except 7686)
38	Head injuries	800, 840
39	Fractures (except of skull)	841-845
40	Acute poisoning	90-92
41	Burns	93
42	Other injuries	Rest of 80-96

Mr. L. Moss (Wartime Social Survey) said that the fact that with moderate illness there was some discrepancy between the number of people saying they had suffered from one sample to another, indicated that such factors as memory were likely to be important in getting an accurate picture. One way to deal with this would be to shorten the lapse of time between the interview and the period to which the questions asked, apply. Thus, it might be that reducing the lapse of time to a maximum of two months from the incidence of illness would considerably reduce the discrepancy shown on Dr. Stocks's chart.

Early sampling data showed that the sampling technique itself proved very efficient and that the discrepancy between figures on different dates could not be put down to this, or to the fact that different investigators were at work. The same team of investigators had been engaged on each inquiry.

Dr. V. Freeman (Islington): The measurement of morbidity would be greatly favoured by the establishment of Health Centres under the White Paper proposals since statistical and clerical staff could be made available to the doctors to assist in the proper recording of the work done on a statistically sound basis. At least one of the staff at the Health Centre should therefore be a trained worker, responsible for the medical records and vital statistical tabulation of the work done at the Centre. The attention of the Minister of Health should be drawn to the importance of this aspect and allowance made for the necessary staff when planning the Health Centres.

Dr. Avery Jones (Middlesex) hoped that the new M.R.C. Classification of Diseases would be widely used in hospitals. An adequate classification of diseases was the first essential for clinical research and enabled previous case records to be re-examined. In many hospitals the existing classifications were totally inadequate and much clinical material was lost unless private records were kept. The M.R.C. System had been in use for six months at the Central Middlesex County Hospital where there was an in-patient turnover of 11,000 cases a year and could be applied by clerical staff with a minimum of medical supervision. It had, therefore, a great advantage over the American Logie System.

for kidney pelves. If one cannot have a two-way drainage, as, for example, when one is working through a ureteral catheter, it is necessary to inject the solution manually into the end of the catheter or to use the alternate apparatus, devised by our colleague, Dr. Lawrence Kinsell, and shown in fig. 2. With this apparatus the constant presence of an attendant is required; this attendant can, however, be the patient himself.

If one is dependent entirely on the ureter for the introduction of the fluid, it is preferable to use a soft-rubber catheter (Bardam No. 10) because of the danger of erosion of the ureter after prolonged intubation with a hard-woven catheter. This soft catheter can best be introduced with the help of a fibre stylet; once in position it can be left for weeks (Case VI) or months, if one is to judge by experience with ordinary skin ureterostomies. The problem of keeping the ureteral catheter in place is a somewhat difficult one because of the tendency of the peristalsis of the ureter to displace it. This trouble has been overcome by the apparatus shown in fig. 2.
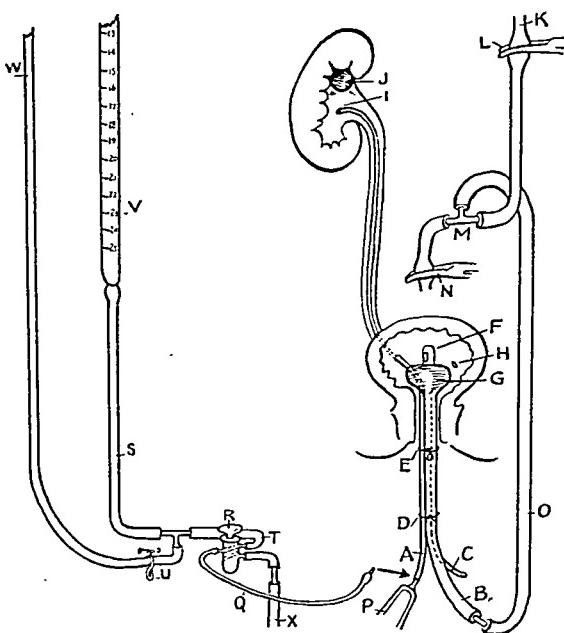
FIG. 2.—Apparatus if dissolution is to be carried out through one ureteral catheter. A—ureteral catheter; B—proximal end of Foley catheter; C—tube through which balloon of Foley catheter is inflated; D and E—sutures fixing ureteral catheter to Foley catheter; F—distal end of Foley catheter; G—balloon of Foley catheter; H—ureteral orifice; I—distal end of ureteral catheter; J—stone; K—tube leading to reservoir of fluid used in bladder irrigation; L—forceps; M—glass T tube; N—forceps on tube leading to waste-fluid bottle; O—rubber tubing; P—syringe through which Solution G is inserted; Q—small-calibre tubing similar to ureteral catheter; R—three-way stopcock; S—tube leading to burette; T—rubber tubing; U—clamp; V—burette; W—end of tube leading to Solution G; X—tube leading to waste bottle. Since it is very irritating to void around a catheter it is necessary to have a bladder catheter as well as a ureteral catheter. A Foley catheter is used since it can be drawn tightly into the bladder neck and thus securely fixed. In this way a fixed object is furnished to which the ureteral catheter can be sewn. To irrigate the bladder one clamps the tube at N and opens the tube at L, thus allowing fluid to go into the bladder; to empty the bladder one opens the tube at N and clamps the tube at L. If the patient is to work the apparatus himself, it is suggested that the apparatus at the left of the diagram is used instead of a syringe. The patient fills the burette to the desired level by opening the clamp U. To put fluid into the kidney tube, the burette is connected through tubes S and T with the small tube Q, by adjusting the three-way stopcock R. To let fluid out of the kidney, tube Q is connected with tube X by turning stopcock R. If a No. 10 Bardam tube is used for the ureteral catheter and for tube Q, the dead space amounts to 3 c.c. for 125 cm. of tubing.

The use of solution "G" to dissolve encrustations on the bladder mucosa has proved very successful. This can be best accomplished by using either a two-way urethral catheter in the bladder, or by using a single catheter with the Munro type of tidal drainage.

Urinary antiseptics such as sulphathiazole should be used in most cases during the period of treatment to reduce or prevent infection.

levulinic acid at pH 4·0. This solution was less irritating, although also less effective, than the original citrate solution at pH 4·0, and was used with success on several clinical cases.

At this time it was found that the addition of magnesium sulphate to this levulinic acid solution greatly decreased the irritability. The difference in the appearance of the bladder irrigated with levulinic acid alone and levulinic acid with magnesium sulphate was striking. Citrate solutions with magnesium were then tested, and the same marked decrease in irritability of the solutions with magnesium was again noted. Whereas citric acid-citrate solution at a pH of 4·0 would produce considerable œdema and hæmorrhage in the bladder mucosa, this same solution plus the magnesium iron had only a slight irritating effect on the bladder mucosa. Many combinations of citrate and magnesium were tried and finally solution "G" was found to be the most practicable formula. The formula of solution "G" is as follows: Citric Acid (monohydrate) 32·25 g.; magnesium oxide (anhydrous) 3·84 g.; sodium carbonate (anhydrous) 4·37 g.; water q.s. ad 1,000 c.c.

The success of stone dissolution depends, of course, on the amount of time the solution is in contact with the stone. Apparatus to be used in each case depends on whether one is working through a simple nephrostomy tube, a two-way nephrostomy tube, two nephrostomy tubes, a ureteral catheter and a nephrostomy tube, or one or more ureteral catheters. Each case demands special mechanical techniques. Since solution "G" is somewhat irritating to about 50% of patients, this factor also has to be considered in devising the apparatus.

When the stones lie in the kidney calices it is desirable that a slight amount of intra-pelvic pressure be obtained to make sure that the solution gets around all the stones. However, the operator should see to it that this pressure is not continuous lest a constant back pressure stir up a pyelonephritis. This means that the solution must in some way be introduced intermittently. Fig. 1 illustrates one possible apparatus to obtain these ends.
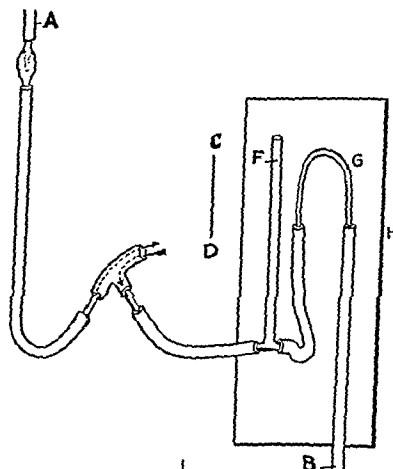
FIG. 1.—Tidal-drainage apparatus to produce intermittent intrapelvic pressure through a two-way nephrostomy tube. A—tube from reservoir of fluid leading to Murphy drip; B—tube leading to waste-fluid; C—level where siphoning begins; D—level of pelvis; E—two-way nephrostomy tube leading to kidney pelvis; F—upright glass tube open at upper end; G—curved glass tube acting as siphon; H—board to which apparatus is fixed. As fluid enters the system from A, the pressure rises until the fluid reaches C, the height of the siphon; at that point, fluid siphons off until air coming into tube F breaks siphon; the whole process then starts over again. The distance, C to D, measures the extent of intrapelvic pressure before the fluid siphons off.

With rare exceptions it is better that the fluid should not go in and out of one tube, as in the Munro tidal-drainage apparatus devised for irrigating so-called "cord bladders". The objection to such an apparatus arises from the fact that the dead space in the tubes is so great in comparison with the cavity being irrigated that a large proportion of the fluid that comes out of the cavity goes back into it again. The efficacy of such a system depends on the ratio of the volume of the viscus being irrigated to the volume of the dead space (tidal fluid). The Munro apparatus is very satisfactory for bladders but not

a day between 7 a.m. and 7 p.m. The patient used in the neighbourhood of 3,000 c.c. daily and did not experience burning on urination. At the end of ten days the stones were definitely smaller (fig. 3B). Each week thereafter showed further improvement until the stones were entirely dissolved (figs. 3C and 3D). The entire procedure took approximately three months; thereafter the nephrostomy tube was removed. During the time of irrigation the patient received 0·5 g. of sulphathiazole three times daily. He was followed in the out-patient department for one year. At the end of that time *P. vulgaris* infection was no longer present: the urine contained some colon bacilli but was acid; a pyelogram showed no recurrence, and the patient resumed his work as a radio engineer.

CASE II.—*A man with a long history of recurring bilateral calcium phosphate stones; many operations; ætiology of original stones obscure, possibly kinked ureters; more recent ætiology, infection with urea-splitting organisms; dissolution with solution "G" through bilateral two-way nephrostomy tubes of those stones in contact with kidney pelves.*

FIG. 4.—Roentgenogram in Case II before (A), during (B) and after (C) attempted dissolution. Note that the stones which dissolved did so completely and that those that did not dissolve remained as they were, because of lack of contact with the solution.

FIG. 5.—Further roentgenograms in Case II to show advantage of an air pyelogram (B) over a pyelogram with opaque substance (A). In B note that the air does not extend down to the stone in the left lower quadrant of the picture but merely goes as far as the arrow

CLINICAL RESULTS

Solution "G" has been used on approximately 25 patients. Eight cases have been selected to illustrate certain points.

CASE REPORTS

CASE I.—*Long history of recurring bilateral calcium phosphate stones; ætiology of first stones probably hypercalcinuria from immobilization and resulting atrophy of disuse; ingestion of milk and of calcium gluconate were added factors; stones on right dissolved with solution "G" through nephrostomy tube.*

In 1928, W. L. (No. 70740), at the age of 18, fractured his left femur and humerus. Because of non-union he was immobilized in bed for six months, and given large amounts of milk and calcium gluconate by mouth. Bilateral renal stones developed, for which there was adequate reason. (Immobilization alone produces marked hypercalcinuria; to this was added a very high calcium intake from the milk and the calcium gluconate. The fallacy of this procedure lay in the fact that there was no point in giving a high calcium intake since non-union of fractures is due to lack of formation of a callus, not to lack of calcification of a callus.) Left pyelolithotomy was performed but *the stone was not analysed*. Nine years later the patient again entered the hospital with bilateral stones; a right nephrolithotomy and a right nephrostomy were performed. When the present studies were started he had been wearing a nephrostomy tube for four years and some large stones had formed in the right kidney (fig. 3A). The serum calcium and

FIG. 3.—Roentgenograms of Case I before (A), during (B and C) and after (D) dissolution of stones. In B, note that the small stone above the catheter has entirely disappeared and that the large stones below the catheter are much smaller; in D, note that the small residual shadow indicated by the arrow lies outside of the kidney pelvis, since air in the lower calix does not extend to the shadow.

phosphorus values were normal; the urine showed *Proteus vulgaris* on culture, which was probably the cause of the recurrent stone.

Solution "G" was introduced through the nephrostomy tube and allowed to pass out through the ureter, bladder and urethra. The solution ran approximately nine hours

FIG. 6.—Roentgenograms in Case IV. A—air pyelogram before dissolution; note the granular centre and the less dense cortex of stone. B—stone after ten days of dissolution; note that the cortex has disappeared and that the remainder of stone has a granular appearance suggesting that it is an oxalate stone. C—larger magnification of A. D—a second roentgenogram of stone at same stage as B with better X-ray technique to bring out the oxalate structure.

This case illustrates the importance of careful X-ray technique in order to rule out oxalate stones; had it been known, as it could have been, that the centre of the stone was definitely oxalate, the procedure would not have been attempted. As a matter of fact, the patient's symptoms were very much improved as a result of the procedure, and it is barely possible that the size of the stone was sufficiently reduced so that it may eventually be passed.

CASE V.—*Left kidney removed for calculus pyonephrosis; remaining kidney totally blocked by right renal stone requiring emergency nephrostomy; stones completely dissolved with solution "G"; bladder irritability overcome by closed urethral drainage.*

C. W. (No. 339467), female aged 25, was perfectly well until one-and-a-half years prior to admission. At that time during her second pregnancy, she developed pyelitis. One year before admission she underwent a left nephrectomy because of calculous pyonephrosis. Six months later she had right renal colic and passed a stone. *None of the stones had been analysed.* Four weeks prior to admission she developed complete anuria of forty-eight hours' duration and attempts at ureteral catheterization were unsuccessful. A right nephrostomy was performed. The patient recovered from the operation and came under our control three weeks post-operatively. The wound was well healed, the nephrostomy tube was draining well, and she was passing nothing from the bladder. The blood calcium and phosphorus were within normal limits. The urine was alkaline and contained large amounts of pus, culture showed *Staphylococcus aureus* and a non-hæmolytic streptococcus. An air pyelogram revealed a stone 2 cm. in diameter in the right uretero-pelvic junction and several small stones in the lower calix (fig. 7A). These had the characteristic X-ray appearance of calcium phosphate stones. An attempt was made to ascertain the patency of the ureter at this time, but it was quite difficult to get liquid or air into the kidney pelvis. As salt solution was dripped into the nephrostomy tube it leaked out around the tubing. The lower calix and infundibulum were apparently

J. S. (No. 308796), in 1925, at the age of 17, developed stones in the left kidney, for which a left nephrolithotomy was performed. In 1937, bilateral stones were found; in 1938 a right nephrolithotomy and a right nephrostomy were performed and in 1939 a left nephrolithotomy and a left nephrostomy. The patient was referred to the Massachusetts General Hospital by Dr. Leo E. Gibson of Syracuse, New York.

The serum calcium and phosphorus levels were normal; the urine was constantly alkaline and contained *Escherichia coli* and a non-hæmolytic streptococcus: the analysis of a stone that had been removed previously showed it to be pure calcium phosphate. Large bilateral stones were present (fig. 4A). As the ureters were practically non-patent, it was impossible to use them for draining out the solution; consequently the nephrostomy tubes were connected to a modified Munro tidal-drainage system. This was without effect because of the large amount of dead space (see p. 31). Therefore the simple nephrostomy tubes were replaced with two-way nephrostomy tubes and solution "G" was allowed to run into one side and out the other. The patient ran approximately 1,500 c.c. of the solution through each tube daily. Figs. 4B and 4c show the dissolution of the stones that were in contact with the kidney pelves. Figs. 5B and 5c show the advantage of an air pyelogram for demonstrating the relation of the stones to the kidney pelvis. Unfortunately complete contact with the stones could not be made (fig. 5B), so that the patient was discharged with a few fragments still remaining and sent back to work with nephrostomy tubes left in place.

CASE III.—*Attempted dissolution with solution "G" through a nephrostomy tube of a stone not found at operation; difficulty with bladder irritability, which was finally overcome.*

J. D. (No. 236588), male aged 41, entered with two stones in the left kidney pelvis and congenital absence of the right kidney. The serum calcium and phosphorus values were normal; the blood non-protein nitrogen was slightly elevated. A left pyelolithotomy was performed but only one stone was found; accordingly a nephrostomy tube was left in place. An analysis of the removed stone showed it to be calcium phosphate. Two weeks after the operation solution "G" was introduced into the pelvis through a nephrostomy tube at the rate of 40 to 60 drops per minute, but caused marked irritability when it reached the bladder. The patient was then cystoscoped and a soft-rubber ureteral catheter was passed to the kidney pelvis; solution "G" was then introduced into this catheter and allowed to come out the nephrostomy tube. The stone was readily dissolved.

CASE IV.—*Recurrent stones due to hyperparathyroidism; removal of parathyroid tumour, leaving residual stone in right kidney; stone stationary in size for a long period of time; then rapid growth following infection with* P. vulgaris (B. proteus); *dissolution of calcium phosphate cortex, with no change in calcium oxalate centre, an outcome that could have been foreseen by X-ray studies.*

J. B. (No. 117408), female, had a right nephrolithotomy in 1938 at the age of 25; the stone was found to contain a large amount of phosphate and a moderate amount of oxalate. The serum calcium was high (12·1 mg. per 100 c.c.), the serum phosphorus was low (2·7 mg. per 100 c.c.), and a diagnosis of hyperparathyroidism was made. A parathyroid tumour was removed by Dr. Oliver Cope. There remained a small stone in the right kidney at the time of the parathyroid operation; this continued constant in size for the next three years. In June 1941, however, the patient was cystoscoped in an outside hospital and developed an infection with *P. vulgaris.* Thereafter the stone grew rapidly.

Although the centre of the stone in X-ray films looked suspiciously like that of an oxalate stone, it was decided to attempt dissolution through a ureteral catheter. A No. 5 whistle-top catheter was introduced into the right kidney pelvis and left in for twenty-four hours, during fourteen of which 5 c.c. of solution "G" were introduced every five minutes. This catheter did not work very well, however, and the patient complained of pain; accordingly it was withdrawn and a No. 10 Garceau catheter was passed. 5 c.c. of solution "G" were injected into this catheter every five minutes for approximately fourteen hours a day for three days. The Garceau catheter was then withdrawn and a No. 10 soft-rubber catheter was introduced. The irrigation was continued for six more days. Fig. 6A shows the stone before irrigation, and fig. 6B after approximately ten days of irrigation. It will be noted that the cortex of the stone was entirely dissolved. By more careful X-ray technique it was then demonstrated that the residual stone was calcium oxalate (fig. 6D).

an infection in the urine with the urea-splitting organism. *Staph. albus,* and was unable to acidify her urine. The phenolsulphonphthalein excretion was excellent, but the urine concentration failed to rise above a specific gravity of 1,012.

After the removal of the parathyroid adenoma the serum calcium and phosphorus values returned to normal, but otherwise there was no change in the patient's condition. To be sure, the urinary calcium excretion fell from a normal level (about 90 mg. in twenty-four hours) to a low level (about 35 mg. in twenty-four hours). During the next five years she was followed in the out-patient department. The staghorn stones remained constant in size; the kidney function remained relatively unaltered. Small calculi were passed from time to time; these presumably were new stones due to the persistently alkaline urine. ·

On April 21, 1942, an inlying soft-rubber catheter was introduced into the right kidney pelvis and dissolution of the stone with solution "G" was started. The apparatus employed is shown in fig. 2. Two nurses were obtained, one for each of two eight-hour shifts; it was their duty to introduce solution "G" by a syringe into the catheter every four to ten minutes, to allow the solution to remain in the kidney two or three minutes, and finally to let it drain from the kidneys. As the stones dissolved away it was possible of course to introduce more fluid at a time; the largest amount used was 30 c.c. The results are shown in fig. 8.

FIG. 8.—Roentgenograms in Case VI. A—before irrigation ; B, C and D—eleven, twenty and forty days, respectively, after onset of irrigation. Note that dissolution proceeded most rapidly in the calices. This was an unexpected result since it was feared that calix stones would be the last to disappear.

FIG. 7.—Roentgenograms in Case V. A—air pyelogram showing stones before dissolution. B—air pyelogram showing stone in lower calix completely dissolved. C—air pyelogram showing all stones dissolved. D—pyelogram with opaque substance to compare with air pyelogram C.

partially blocked by stone and mucus. By means of the Murphy drip apparatus we were finally able to run in solution "G" very slowly. It was as if an exit for the fluid had to be dissolved out first. However, the lower calix stone dissolved and the large pelvic stone began to crumple (fig. 7B); later the larger stone completely disappeared (fig. 7c). The patient had considerable bladder irritability once the solution began going through to the bladder. This complication was managed very easily by placing her on closed urethral drainage. Once she began to tolerate about 2,000 c.c. of fluid per day, the stone dissolved in about ten days. Fig. 7c is an air pyelogram showing that all the stones were dissolved. Fig. 7D is a neoskiodan pyelogram showing that, although there was still moderate hydronephrosis, the ureteropelvic junction and ureter became patent. The right nephrostomy tube was removed, and the patient began to pass clear urine.

CASE VI.—*A fifteen-year history of kidney stones, including right nephrotomy; a diagnosis of hyperparathyroidism made, and a parathyroid adenoma removed; bilateral staghorn stones and pyelonephritis persisted; dissolution of stone on left through ureteral catheter.*

E. R. (No. 135241), female aged 49, married, first developed urinary symptoms at the age of 30. Three years later the late Dr. Arthur Chute removed three "alkaline stones" from the right kidney pelvis. Eleven years later she was referred to the clinic by Dr. Harvard H. Crabtree because of bilateral staghorn kidney stones. Since there were hypercalcæmia (serum calcium, 12·8 mg. per 100 c.c.) and hypophosphatæmia (serum inorganic phosphorus, 2·3 mg. per 100 c.c.), a diagnosis of hyperparathyroidism was made. A parathyroid adenoma was removed by Dr. Oliver Cope in June 1938. (This patient was one of the two in the series of 68 patients with proved hyperparathyroidism who did not have an abnormally high calcium excretion in the urine when first seen.) She had

an infection in the urine with the urea-splitting organism, *Staph. albus,* and was unable to acidify her urine. The phenolsulphonphthalein excretion was excellent, but the urine concentration failed to rise above a specific gravity of 1,012.

After the removal of the parathyroid adenoma the serum calcium and phosphorus values returned to normal, but otherwise there was no change in the patient's condition. To be sure, the urinary calcium excretion fell from a normal level (about 90 mg. in twenty-four hours) to a low level (about 35 mg. in twenty-four hours). During the next five years she was followed in the out-patient department. The staghorn stones remained constant in size; the kidney function remained relatively unaltered. Small calculi were passed from time to time; these presumably were new stones due to the persistently alkaline urine. •

On April 21, 1942, an inlying soft-rubber catheter was introduced into the right kidney pelvis and dissolution of the stone with solution "G" was started. The apparatus employed is shown in fig. 2. Two nurses were obtained, one for each of two eight-hour shifts; it was their duty to introduce solution "G" by a syringe into the catheter every four to ten minutes, to allow the solution to remain in the kidney two or three minutes, and finally to let it drain from the kidneys. As the stones dissolved away it was possible of course to introduce more fluid at a time; the largest amount used was 30 c.c. The results are shown in fig. 8.

FIG. 8.—Roentgenograms in Case VI. A—before irrigation ; B, C and D—eleven, twenty and forty days, respectively, after onset of irrigation. Note that dissolution proceeded most rapidly in the calices. This was an unexpected result since it was feared that calix stones would be the last to disappear.

FIG. 7.—Roentgenograms in Case V. A—air pyelogram showing stones before dissolution. B—air pyelogram showing stone in lower calix completely dissolved. C—air pyelogram showing all stones dissolved. D—pyelogram with opaque substance to compare with air pyelogram C.

partially blocked by stone and mucus. By means of the Murphy drip apparatus we were finally able to run in solution "G" very slowly. It was as if an exit for the fluid had to be dissolved out first. However, the lower calix stone dissolved and the large pelvic stone began to crumple (fig. 7B); later the larger stone completely disappeared (fig. 7c). The patient had considerable bladder irritability once the solution began going through to the bladder. This complication was managed very easily by placing her on closed urethral drainage. Once she began to tolerate about 2,000 c.c. of fluid per day, the stone dissolved in about ten days. Fig. 7c is an air pyelogram showing that all the stones were dissolved. Fig. 7D is a neoskiodan pyelogram showing that, although there was still moderate hydronephrosis, the ureteropelvic junction and ureter became patent. The right nephrostomy tube was removed, and the patient began to pass clear urine.

CASE VI.—*A fifteen-year history of kidney stones, including right nephrotomy; a diagnosis of hyperparathyroidism made, and a parathyroid adenoma removed; bilateral staghorn stones and pyelonephritis persisted; dissolution of stone on left through ureteral catheter.*

E. R. (No. 135241), female aged 49, married, first developed urinary symptoms at the age of 30. Three years later the late Dr. Arthur Chute removed three "alkaline stones" from the right kidney pelvis. Eleven years later she was referred to the clinic by Dr. Harvard H. Crabtree because of bilateral staghorn kidney stones. Since there were hypercalcæmia (serum calcium, 12·8 mg. per 100 c.c.) and hypophosphatæmia (serum inorganic phosphorus, 2·3 mg. per 100 c.c.), a diagnosis of hyperparathyroidism was made. A parathyroid adenoma was removed by Dr. Oliver Cope in June 1938. (This patient was one of the two in the series of 68 patients with proved hyperparathyroidism who did not have an abnormally high calcium excretion in the urine when first seen.) She had

CASE VIII.—*A long history of chronic bladder neck obstruction associated with bladder encrustations; this required repeated transurethral resections and removal of calcified debris and stones; constant irrigation with solution "G" through double type urethral catheter completely dissolved encrustations.*

This 60-year-old man entered the hospital with a history of frequency and dysuria; he complained of passing bits of chalky material in his urine. Two years previously and one year previously he had undergone transurethral resections at which times small amounts of bladder encrustations and stones were removed with a lithotrite. At this admission the patient was cystoscoped and panendoscoped. The bladder outlet appeared normal but there were many encrustations throughout the bladder, chiefly in the region of the trigone. The urine was cloudy, strongly alkaline, and loaded with pus. The urethra was catheterized with a No. 22 soft-rubber double catheter. Solution "G" was allowed to drip continuously through a Murphy bulb system into the inlet of the double catheter. This procedure was continued forty-five minutes of each hour for twelve hours daily. After six days of such irrigations, the calcified material had been dissolved and the patient's bladder mucosa appeared relatively normal as shown in fig. 10.

SUMMARY AND CONCLUSIONS

Citrate solutions with magnesium are practicable for the dissolution of urinary calculi composed of calcium phosphate, calcium carbonate, and magnesium ammonium phosphate. Six selected cases of kidney stones and one case of bladder encrustation are presented in which the solution was used successfully for the partial or complete dissolution of the stones. In two cases the solution was introduced into the kidney pelvis through a ureteral catheter; one case is reported in which attempted dissolution of a large stone was without success because the solution was prevented from coming in contact with the stone by a thin coating of unidentified material, possibly old blood clot or fibrin.

The type of apparatus to be used depends on the individual case. Attempts should be made to prevent too great an intrapelvic pressure in the kidney for too long a period of time. For determining whether a stone is in contact with the kidney pelvis and for following the course of dissolution, an air pyelogram is the method of choice. Since solution "G" has no effect on calcium oxalate, uric acid, or cystine stones, careful study of roentgenograms, stone analysis, and circumstantial evidence is most important before treatment is started.

REFERENCE

ALBRIGHT, F., SULKOWITCH, H. W., and CHUTE, R. (1939) *J. Amer. med. Ass.*, **113**, 2049.

Professor E. C. Dodds: I have listened to Captain Suby's paper with the greatest of interest and congratulate him on the excellent results he has obtained. Speaking as a laboratory worker who has analysed many calculi, I have always been impressed on cutting a calculus with the amount of protein material on the surface of the calculus and the interstices. I wonder whether the failure in some of the cases reported by Captain Suby might be due not only to the fluid in reaching the calculus, but actually to its inability to penetrate the protein film on the surface. For some curious reason it is little known that strong urea solutions are capable of dissolving proteins with the greatest of ease; I wondered if Captain Suby has thought of the possibility of adding urea to his solution? I trust the members of the Section will realize that I am speaking purely from an *in vitro* standpoint. I naturally have no idea as to what effect high concentrations of urea would have on tissues of the body.

Wing Commander J. C. Ainsworth-Davis (*in absentia*): I have been using this solution in a number of patients with *renal* calculi, and have devised a two-way self-retaining ureteric catheter for the purpose of continuous pelvic lavage.

It consists of two No. 4½ degree Charrière ureteric catheters of unequal lengths, welded together so that the tip of the longer projects some 1½ in. beyond that of the shorter. A fine wire passes through the shorter catheter and is attached to the tip of the longer.

CASE VII.—*Bilateral calcium phosphate and carbonate stones; ætiology probably excessive intake of sodium bicarbonate and cheese; left nephrectomy and right nephrostomy performed previously; attempt to dissolve stone in right kidney through ureteral catheter; cause of failure shown by X-ray study.*

R. W. (No. 354198), a 47-year-old, married woman, was admitted because of right renal stone. A left nephrectomy and right nephrostomy had been performed one year previously. The patient was for a long time in the habit of ingesting large amounts of sodium bicarbonate and cheese. Stones removed at two previous operations contained large amounts of calcium phosphate and calcium carbonate. The last stone removed from the right kidney was noted in addition as having a peculiar coating, the exact nature of which was not determined but which was thought to be clotted blood since it gave a strongly positive guaiac test. The serum calcium and phosphorus levels were within normal limits. A ureteral catheter was introduced into the right kidney pelvis and irrigations were carried out as in Case VI. Re-examination six days later showed no decrease in the size of the stone. Failure was undoubtedly due to the capsule of organic material surrounding the stone, which prevented its solution (figs. 9A and 9B).

FIG. 9.—Roentgenograms in Case VII. A—stone before attempted dissolution. B—pyelogram with opaque substance after failure to dissolve the stone. Note that the stone is coated with some substance that prevents the opaque material from coming in contact with it.
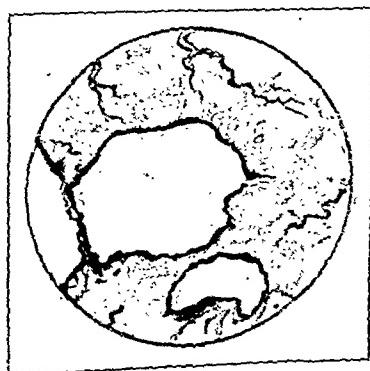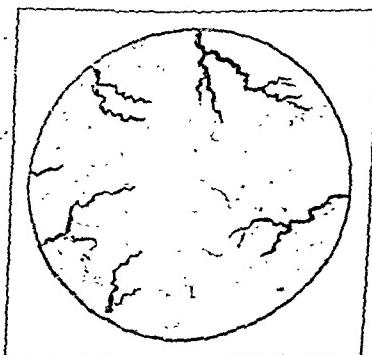
(a)   (b)

FIG. 10.—Cystoscopic appearance of bladder in Case VIII: (a) before treatment with solution "G"; (b) after treatment with solution "G".

JOINT DISCUSSION No. 5

Section of Surgery with Section of Medicine

Chairman—Sir JAMES WALTON, K.C.V.O., M.S.

(President of the Section of Surgery)

[*May* 3, 1944]

DISCUSSION ON PERIPHERAL VASCULAR LESIONS

Dr. Geoffrey Evans in his opening of the discussion excluded arterial obstruction due to trauma and external pressure: inflammatory diseases of the arteries of known causation: conditions characterized by vasodilatation and immersion injuries. This left for his consideration Raynaud's disease, thrombo-angiitis obliterans (Buerger's disease) and arteriosclerosis, which he subdivided into the hypertensive type, the senile type, and either of the above complicated by diabetes mellitus.

Dr. Evans compared these three main groups of arterial disease in terms of vasospasm, especially prominent in Raynaud's disease, endothelial proliferation, thrombosis, a cardinal feature of Buerger's disease, and the intermittent course characteristic of all. In his remarks about treatment Dr. Evans called attention to the first importance of eliminating vasoconstrictor drugs, including ergot and its preparations, adrenaline, ephedrine, benzedrine and tobacco. He spoke of tobacco sensitization, the necessity for every patient with peripheral vascular disease to give up smoking altogether, and he reported an illustrative case of severe pain in the lower extremities with intermittent claudication, a woman aged 53, B.P. 190/106, who recovered when she stopped smoking. As to vasodilator drugs, Dr. Evans referred especially to aspirin and alcohol, and claimed symptomatic relief of real value in certain cases by the continued use of papaverine sulphate. He also referred to the use of thyroid extract. In the third place Dr. Evans went into some detail on the subject of over-fatigue, whether emotional or physical, as an undoubted cause of peripheral vasoconstriction. He then described treatment in its general aspects from the point of view of the patient as a whole with special reference to anæmia, digestive disorder and sleeplessness, and the need to correct organ or system dysfunction by all means possible. Lastly, Dr. Evans described various forms of physiotherapeutic treatment, and showed an apparatus for the production of intermittent venous occlusion, which has on occasion proved extremely beneficial. This apparatus was invented by Dr. Martin Wright, and has been modified and improved by Mr. Schranz of the Genito-Urinary Co., and after the war this apparatus, Dr. Evans said, would be available for general use.

Professor E. D. Telford: The operations for sympathectomy are two. For the upper limb a section of the thoracic chain at or just below the neck of the third rib with dislocation of the cut ends to prevent reunion. For the lower limb, an excision of the lumbar chain for a length of one and a half to two inches centred opposite the body of the 3rd lumbar vertebra. Owing to the inconstant anatomy of the lumbar chain it is not possible to define this operation in terms of ganglia. Both these operations are preganglionic sections.

Sympathectomy will abolish or reduce spasm, and will dilate collateral channels if it be still possible for these to dilate. Other results such as the healing of ulcers and abolition of pain are of course the result of the improved blood supply; there is no question of interruption of afferent fibres.
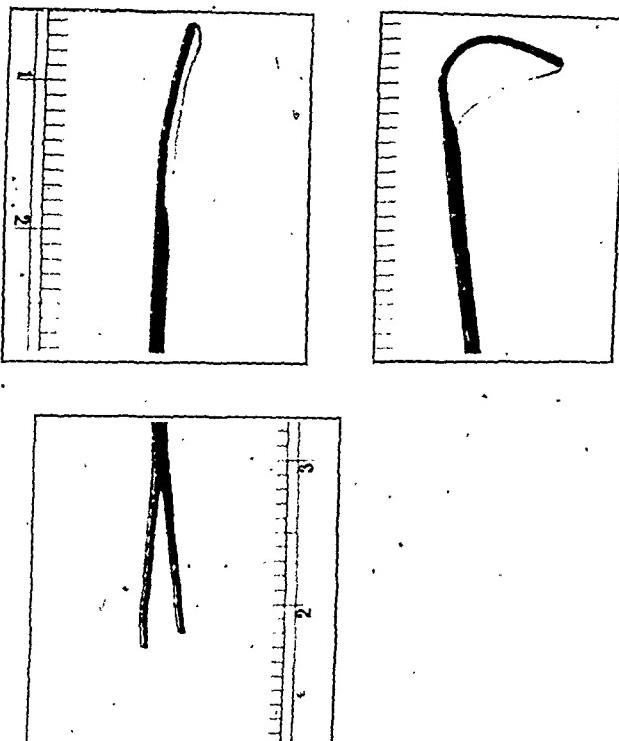
This two-way catheter is passed in the ordinary way through an operating cystoscope under pentothal anæsthesia, to the pelvis of the affected kidney, where, on pulling the wire, it becomes self-retaining (fig. 1). After removing the cystoscope, an Andrews' pyelography nozzle is securely wedged into the shorter catheter, which effectively holds the wire in position, and through this the irrigating solution is run in at the rate of 60 drops to the minute. The outflow is through two lateral holes in the longer component.

Every third day solution "G" is replaced by a 0·5% solution of urease for a few hours to remove organic material. The two-way self-retaining catheter has been made for me by Donald Rose of 36, George Street. W.1, and I hope that it will afford some slight help in the solution of certain forms of renal calculi.

delayed till twelve or even eighteen months. Even with relapse it is seldom that the patient says it is as bad as before; usually they are satisfied because the attacks are less frequent, less easily provoked and never as prolonged or severe. What is the explanation of this?

Some observers say it is local arterial disease. Simmons after long and very careful work in my clinic thought regeneration the likely cause. I think regeneration is unlikely owing to the radical measures taken to prevent it and on two occasions I have had the chance at a second operation to inspect the area some years afterwards and have found no sign of regeneration. To my mind the explanation lies in the great variations in anatomy. Sheehan dissected with meticulous care 25 stellate ganglia and found no two alike in the pattern of their connexions. I have watched for some years two patients in each of whom an identical operation was done on the two sides. In each of these patients one hand remains perfect, the other has relapsed badly.

In this connexion the facts of the disease in the feet are significant. Admittedly although common in the feet it is not often severe and seldom causes incapacity. I have, however, had 22 patients who were unable to work from the consequences of the disease in the feet. Every one of these is completely cured and remains well after lumbar sympathectomy. The explanation may be that in the lumbar operation the section of the chain is complete and certain; it is preganglionic for the sacral ganglia and is so high above them that variations in their individual anatomy are of no account.

ACROSCLEROSIS

Closely associated with the Raynaud phenomenon is the crippling and distressing condition of acrosclerosis or sclerodactyly. Some writers deny its association with the true Raynaud's disease of young women but from my own observation I have no doubt that it can follow the disease.

In an effort to relieve the claw-like contractures of the fingers and the constant painful ulceration of their atrophic pulps I have tried out the operation in 19 patients but the results have been very disappointing. In two cases only, and these the earlier types, has the operation seemed to check further deterioration and allowed the patient to return to work. Sympathectomy is useless in the more advanced cases. The only hope lies in a better knowledge of the cause and of the treatment of the initial Raynaud phenomenon.

The like unsatisfactory results have followed sympathectomy in the grave condition of dermatomyositis. In three patients in whom both lumbar and thoracic sections were done the progress of the disease was unaffected.

THROMBO-ANGIITIS OBLITERANS

This disease and arteriosclerosis are responsible for the majority of occlusive arterial troubles and the differential diagnosis is not always an easy one. If the onset of symptoms is first noticed in the twenties the trouble is almost certainly thrombo-angiitis. In the thirties although a few cases of arteriosclerosis are found the diagnosis of thrombo-angiitis is highly probable but in the forties a diagnosis of arteriosclerosis is more likely to be correct. The decade 30 to 40 is a period of overlap between the diseases but after 50 I should regard a diagnosis of thrombo-angiitis with grave suspicion.

The factors in the differential diagnosis are the ordinary clinical signs of arteriosclerosis, X-ray evidence of calcification and the extreme rarity of thrombo-angiitis in women. Examination of the popliteal fossa is important; the periarteritis of thrombo-angiitis produces a hard, diffuse, fibrous mass never seen in arteriosclerosis.

It is not easy to estimate the results of sympathectomy or indeed of any other treatment in thrombo-angiitis. The prognosis is very variable and there are long quiet periods.

There are broadly speaking two types. The one found in the early twenties and often ushered in by the Raynaud phenomenon has a grave prognosis. The other beginning in older patients is much more chronic and may exist for long periods without much deterioration.

My own results are 85 patients operated upon for thrombo-angiitis of the lower limbs. Of these 11 are untraced leaving 74. Of these 37 are regarded as good, 13 as fair and 24 are failures many of whom, and these mainly the younger men, have come to amputation.

In some of the younger patients the disease is found in the arms usually some years after its appearance in the legs. I have done thoracic sympathectomy for seven of these cases and have watched several of them for some years. The progress of symptoms seems to have been arrested and the worst that has happened is that four patients have suffered partial amputation of one or more fingers.

Spasm is the main factor in some diseases such as the various types of the Raynaud phenomenon though I cannot but think that its presence and action have in other forms of vascular disease been invoked too often on scanty or mistaken evidence.

For example, if a man suffering from occlusive arterial disease be asked to walk a few yards and his feet are then examined they will be found cold and blanched. This is not, as has often been assumed, evidence of spasm. The explanation is that his veins, notably assisted by the muscular action, have carried off the blood much more rapidly than it can be replaced by the embarrassed arteries. An identical result is obtained if the limb be raised above heart level for a few seconds and the rapidity of this blanching is the most valuable guide we have to the extent of the arterial damage.

Unfortunately the abolition of spasm seen after sympathectomy is neither total nor permanent. The relapses are two: (1) Immediate, and (2) Deferred. The immediate relapse which is only a partial one is seen in all cases five or six days after the operation. It takes the form of some loss of colour and heat and is probably due to autonomic action of smooth muscle. The deferred relapse is fairly common. It comes on at periods of six to eighteen months after operation and will be discussed in its relation to the results of sympathectomy in the Raynaud phenomenon.

It is to the second effect of sympathectomy, i.e. vasodilatation, that the beneficial results are mainly due. These results must depend upon the extent and area of the thrombosis. Fortunately we have in spinal anæsthesia or nerve block a simple and accurate means to estimate the results likely to be given by sympathectomy.

Effective vasodilatation is responsible for the relief of pain which in many cases is so welcome a feature of the operation. Pain in chronic vascular disease is the outstanding trouble. It may be divided into two groups: (1) exercise pain, and (2) rest pain.

As regards the exercise pain (intermittent claudication) the results of sympathectomy are disappointing. Full recovery is very rare but it is more common to find that some patients state that their walking distance is slightly increased and that the cramp passes off more quickly. In the majority little or no improvement is seen. I do not think that any surgeon is justified in promising that the operation will cure claudication.

It is different with the rest pain. This is a pain coming on later in the course of the disease; a starvation pain due to increasing digital thrombosis. It is associated with rubor which gradually deepens into a persistent cyanosis and the picture is one of impending gangrene. In many such cases the results of sympathectomy are most satisfactory and the relief of pain is dramatic. Everything depends upon the extent of the thrombosis; if some degree of vasodilatation is still possible the result will be satisfactory. Hence the operation should be done early in cases where rest pain is present.

RESULTS

The number of patients in my Clinic who have been operated upon for peripheral vascular lesions is 436. Nearly all have had bilateral operations and in some the thoracic and lumbar sections have been done in the one patient. Thus the number of limbs available for study is considerable. Of these 436 cases I exclude 57 as having been operated upon within the last year. The estimation of the result of a sympathectomy should not be made until at least twelve months have passed. There were three deaths in the series—one from alcoholic delirium, one from pulmonary embolus and one from hæmatemesis from an unsuspected duodenal ulcer. The follow-up has been very thorough and the number of cases untraced is small.

I have classified the results as: good, fair, and failed. By good I mean relief of pain, healing of ulcers and gangrene and, what is after all the real touchstone, ability to return to work. By fair I mean that some improvement or alleviation has been obtained; the patient says the operation has been worth while. Failed explains itself and not infrequently means amputation for gangrene. But it is fair to point out that as the result of the sympathectomy it is nearly always possible to get away with a below-knee amputation instead of the customary lower third of thigh; this is a great gain to the patient.

I have then to consider 376 patients under the various disease headings and I begin with

THE RAYNAUD PHENOMENON

This class provides at once the most interesting and the most disappointing results. In the Raynaud lesion affecting the hands my own operated patients are 41 of whom 16 are classified as good, 8 as fair, and 13 as failed with 4 untraced. In each case the operation has been the same and in every patient the immediate result has been a full vasodilatation and an apparently most gratifying cure. Yet only 16 out of 37 remain well some years afterwards. The relapses occur as early as six months but may be

delayed till twelve or even eighteen months. Even with relapse it is seldom that the patient says it is as bad as before; usually they are satisfied because the attacks are less frequent, less easily provoked and never as prolonged or severe. What is the explanation of this?

Some observers say it is local arterial disease. Simmons after long and very careful work in my clinic thought regeneration the likely cause. I think regeneration is unlikely owing to the radical measures taken to prevent it and on two occasions I have had the chance at a second operation to inspect the area some years afterwards and have found no sign of regeneration. To my mind the explanation lies in the great variations in anatomy. Sheehan dissected with meticulous care 25 stellate ganglia and found no two alike in the pattern of their connexions. I have watched for some years two patients in each of whom an identical operation was done on the two sides. In each of these patients one hand remains perfect, the other has relapsed badly.

In this connexion the facts of the disease in the feet are significant. Admittedly although common in the feet it is not often severe and seldom causes incapacity. I have, however, had 22 patients who were unable to work from the consequences of the disease in the feet. Every one of these is completely cured and remains well after lumbar sympathectomy. The explanation may be that in the lumbar operation the section of the chain is complete and certain; it is preganglionic for the sacral ganglia and is so high above them that variations in their individual anatomy are of no account.

ACROSCLEROSIS

Closely associated with the Raynaud phenomenon is the crippling and distressing condition of acrosclerosis or sclerodactyly. Some writers deny its association with the true Raynaud's disease of young women but from my own observation I have no doubt that it can follow the disease.

In an effort to relieve the claw-like contractures of the fingers and the constant painful ulceration of their atrophic pulps I have tried out the operation in 19 patients but the results have been very disappointing. In two cases only, and these the earlier types, has the operation seemed to check further deterioration and allowed the patient to return to work. Sympathectomy is useless in the more advanced cases. The only hope lies in a better knowledge of the cause and of the treatment of the initial Raynaud phenomenon.

The like unsatisfactory results have followed sympathectomy in the grave condition of dermatomyositis. In three patients in whom both lumbar and thoracic sections were done the progress of the disease was unaffected.

THROMBO-ANGIITIS OBLITERANS

This disease and arteriosclerosis are responsible for the majority of occlusive arterial troubles and the differential diagnosis is not always an easy one. If the onset of symptoms is first noticed in the twenties the trouble is almost certainly thrombo-angiitis. In the thirties although a few cases of arteriosclerosis are found the diagnosis of thrombo-angiitis is highly probable but in the forties a diagnosis of arteriosclerosis is more likely to be correct. The decade 30 to 40 is a period of overlap between the diseases but after 50 I should regard a diagnosis of thrombo-angiitis with grave suspicion.

The factors in the differential diagnosis are the ordinary clinical signs of arteriosclerosis, X-ray evidence of calcification and the extreme rarity of thrombo-angiitis in women. Examination of the popliteal fossa is important; the periarteritis of thrombo-angiitis produces a hard, diffuse, fibrous mass never seen in arteriosclerosis.

It is not easy to estimate the results of sympathectomy or indeed of any other treatment in thrombo-angiitis. The prognosis is very variable and there are long quiet periods.

There are broadly speaking two types. The one found in the early twenties and often ushered in by the Raynaud phenomenon has a grave prognosis. The other beginning in older patients is much more chronic and may exist for long periods without much deterioration.

My own results are 85 patients operated upon for thrombo-angiitis of the lower limbs. Of these 11 are untraced leaving 74. Of these 37 are regarded as good, 13 as fair and 24 are failures many of whom, and these mainly the younger men, have come to amputation.

In some of the younger patients the disease is found in the arms usually some years after its appearance in the legs. I have done thoracic sympathectomy for seven of these cases and have watched several of them for some years. The progress of symptoms seems to have been arrested and the worst that has happened is that four patients have suffered partial amputation of one or more fingers.

The hope which some of us held at the beginning that thrombo-angiitis was a spastic disease capable of arrest by sympathectomy has not been fulfilled. It must be concluded that thrombo-angiitis is a toxic disease of as yet unknown origin in which spasm is purely incidental and that sympathectomy can have no effect on the cause. What satisfactory results it has given are due entirely to improved collateral circulation.

ARTERIOSCLEROSIS

For some years I have observed the results of sympathectomy in the peripheral forms of the disease and am convinced that there is one stage in the downward course in which the operation is well worth while. I would put it in this way. The first symptom is claudication, slowly but inevitably getting worse. For this, as I have already said, sympathectomy can do little. After a time, if the patient's coronary arteries have not given out, he enters on a stage of rest-pain with rubor gradually passing into a persistent and deepening cyanosis of one or more toes. This is the stage at which sympathectomy has given good results. If no operation be done the condition passes into frank gangrene and for this the operation is not worth doing.

I have operated in all on 62 cases of whom three are untraced. This leaves 59. Of these 37 are good, 10 are fair and 12, these mainly the older cases, with definite gangrene, have failed. The average age of the 62 patients is 56 years.

ERYTHROCYANOSIS AND ANTERIOR POLIOMYELITIS

I have bracketed these conditions because from the standpoint of their vascular lesions they are identical. Each of them when severe is liable to develop multiple, hard, deep and painful nodules—the so-called erythema induratum. These nodules may very slowly absorb but often break down into painful and indolent ulcers. The trouble is determined by three factors: excessive fat, poor blood supply and the action of cold. The lesion is a fat necrosis, or more exactly a fat saponification. The nodules and ulcers are, of course, Nature's effort to digest or throw out the soap and in this process giant-cells play an active part. It is the presence of these cells together with the fact that Bazin described the lesion in his lectures on tuberculosis which has caused the disease to be generally, but I believe mistakenly, regarded as tuberculous.

The results of sympathectomy have been very satisfactory and the identity of the two conditions is further borne out by the similarity of these results.

The figures are: Erythrocyanosis, 57 cases with 5 untraced, leaving 52. Of these 39 are good, 6 are fair and 7 have failed.

In anterior poliomyelitis 55 cases with 6 not traced, leaving 49. Of these 40 are good, 4 are fair and 5 have failed.

It should be noted that the failures are all in the older patients with grossly fat limbs.

ACROCYANOSIS

This state of persistently swollen, blue and moist extremities is fairly common but in its more severe form in the hands it may prevent the patient from following such occupations as fishmongering and greengrocery. When it occurs in the feet it may incapacitate workers in dye-houses and breweries. I have operated on 16 of these cases. 7 for the hands and 9 for the feet. The results are, as one would expect, comparable to those found in the Raynaud phenomenon. Of the 7 cases in the hands, 4 only can be regarded as cured, but of the 9 suffering from the trouble in the feet all remain perfectly well.

PERNIOSIS

The occurrence of severe chilblains on the hands or feet of adults is occasionally a cause of inability to work. I have operated upon 11 of these patients, 3 for the hands and 8 for the feet. They have all been cured and remain at their work, one of them in a cold-storage chamber.

ERYTHROMELALGIA

The lesion as described by Weir Mitchell is very rare and the literature shows much confusion with the painful rubor common in the later stages of arterial occlusion. It has, of course, nothing to do with this.

I have treated by sympathectomy five true examples of the disease, including one in a severe polycythæmia rubra vera, in which disease vascular lesions of the lower extremity are not uncommon.

It would appear quite unreasonable to treat by sympathectomy a disease in which the clinical features suggest active vasodilatation but the answer is that it works. All five of my patients were cured at once and remain well.

Dr. Raymond Greene: No one experienced in the effects of cold can fail to be impressed by the fact that in apparently similar circumstances one man will be frostbitten and another not. Yet the question of individual susceptibility has been hardly mentioned by earlier observers. The exceptions are Lewis and Love (1926) who showed that the freezing point of human skin might be anything from −2·2° C. to −25° C. according to the amount of oil in the skin; Lewis again (1941) when he advanced the hypothesis that chilblains are due to a failure of relaxation of the peripheral arterioles; and Block (1944) who drew attention to the influence of autonomic constitution on susceptibility to frostbite on the Russian front. Few seem to remember the thyroid, though everyone is, of course, aware of its part in temperature regulation. Disturbances of this function were among the earliest observed symptoms of thyroid deficiency. In 1932 Dietrich and Schwiegk found that the gland responded rapidly to changes in the temperature of animals, or of the blood in their carotid arteries, by increased activity on cooling and decreased activity on warming. Moreover, the presence of thyroid hormone is necessary for the normal activity of adrenaline, which is so important for temperature regulation.

When the temperature of the blood passing through the thalamic thermosensitive centre is lowered, a number of effects follow. From the present point of view, two are important. Heat loss is reduced by an increased output of adrenaline with consequent constriction of skin vessels, and heat production is increased by stimulation of the thyroid. In deficiency of thyroid secretion, this mechanism may fail. The temperature of the body is low owing to low oxygen consumption, and the thyroid is incapable of responding adequately to a demand that it shall be increased. The body has a habit of overdoing its protective processes. The diabetic, unable to use his sugar, uses his fat with such enthusiasm that he dies of ketosis. The healthy wound granulates to such good effect that epithelialization cannot keep pace. The osteo-arthritic joint, in an attempt to take the strain off its fibrillated cartilage, throws out supporting bastions so large that the joint is immobilized. The heart valve after the attacks of rheumatism heals so well that it becomes stenosed. The hypothalamus of the patient deficient in thyroxin produces in its efforts to conserve the body heat so complete a vasoconstriction that the extremities are rendered more susceptible than they should be to the damaging effects of cold. Even in the absence of excessive cold gangrene may occur.

The general observation that the thyrotoxic patient has hot feet and the myxœdematous cold has been scrutinized in detail by Pickering and Hess (1933), Sheard and Williams (1940) and other workers. Sheard and Williams have measured the loss of heat from various regions of the body and have found that the extremities and especially the feet are the best "radiators". It is on the hands and feet more than on other parts that the thyrotoxic relies to keep his temperature down and it is to their capacity for vasoconstriction that the hypothyroid trusts to maintain his precarious warmth. From this it would be expected that some relation might be found between basal metabolic rate and toe temperature. In fact, as Maddock and Coller (1933) showed, a simple linear relationship exists between the temperature of the big toes and the basal heat production per unit of surface area. Sheard and Williams showed that in 19 other regions no such relationship exists, but in the big toe a drop of 1° C. represented in their experiment a diminution of approximately 1 calorie per sq. metre per hour. This relationship holds with normal, subnormal and supranormal basal metabolic rates.

To illustrate these findings, I wish to draw your attention to a type which is very common in the panel waiting room. The patient is a thin weary girl, with a poor appetite, absent or scanty and irregular menses, and cold slightly cyanosed hands and feet. Her hair is dull and often scanty, her skin dry and chapped. Her pulse-rate is slow. In winter she whines about the weather and looks forward to summer with a pathetic yearning. I remember one whose slum bedroom wall was plastered with a tourist agent's pictures of blue Mediterranean seas and sun-drenched African sands. Were she fat, no one would fail to diagnose hypothyroidism. Because she is thin the diagnosis is frequently missed. The exhibition of thyroid produces only a partial amelioration of her symptoms. Her skin becomes less dry and cold, but her weight does not increase nor her sexual function return. The metabolic error is broader than mere thyroid failure.

It is easy to guess that we are dealing with a common and usually unrecognized *forme fruste* of the comparatively rare disorder anorexia nervosa, in which the effects of thyroid deficiency are seen in their extremest form. This condition illustrates more beautifully than any other the interdependence of the psyche, the autonomic nervous system and the endocrine glands. I have recently had the opportunity to investigate in detail five such cases. I picture the disease as one in which the patient, for reasons best known to herself, decides to give up eating. The body reacts to the lack of fuel by two economies. It discards the sexual function, which is unnecessary for its individual survival, and it damps down its oxygen consumption. We may guess that, by paths which are anatomi-

cally demonstrable, the pituitary ceases its gonad-stimulating and thyroid-stimulating functions, and the patient develops amenorrhœa or impotence and an extreme degree of thyroxin deficiency which reduces the basal metabolic rate to the lowest figures ever found. Because the thyroid itself remains normal, it is inaccurate to speak of hypo-thyroidism. The failure is higher in the scale. The thyroid is no longer stimulated to activity by the pituitary and we should therefore speak rather of hypothyrokinesis.

My patient illustrates this well. Her hands and feet were deathly cold even in the hottest weather, but their temperature could be raised temporarily to normal by the prolonged use of a radiant heat cradle. Her basal metabolic rate (estimated by Dr. Douglas Robertson) was −48. That her condition was not due to hypothyroidism but to hypothyrokinesis is shown by fig. 1, which illustrates the effects of administering the thyroid-stimulating factor of the anterior pituitary.

FIG. 1.

A second patient, a girl of 15, was a case even more severe. Her basal metabolic rate was −51. All extremities, including her nose, were cold and blue. Her left hand was purplish red and stone cold to the touch

The skin of the forefinger was gangrenous, the pulp of the tip shrunken and the nail atrophied. There were small patches of shallow gangrene on all the fingers of the left hand. That this condition was due to arterial spasm was made clear by an ulnar and medial nerve block of the right (the better) hand. The temperature, on a very hot summer afternoon, was 71° F., and rose rapidly after nerve block to 88° F. That the spasm was due to low body temperature is made clear by the temperature and pulse charts. During treatment with thyrogan (fig. 2) great improvement occurred in the right hand,

FIG. 2.

which was previously cold and cyanosed but not gangrenous, but there was little improvement in the gangrenous left hand. The response to heating of the body was also more obvious on the right. The appearance of the capillaries viewed under the microscope is likewise different, the loops on the right being fine but complete and regular, those of the left forefinger irregular in shape and distribution and in places missing altogether. It seems probable that a multiple thrombosis of small skin vessels has occurred in the forefinger of the left hand It is rather remarkable that eighteen months after I unsuccessfully advised sympathectomy as an urgent measure to save the forefinger, it is still blue but still there, the rest of the hand being slightly better, apparently as a result of intensive psychological treatment by Dr. Douglas Macaulay. Her temperature is now normal, she menstruates occasionally and she has put on 1 stone in weight.

I mention these cases briefly in order to draw attention to the fact that lowered thyroid activity commonly produces not merely cold extremities, but the *very* cold and cyanosed extremities which are sometimes labelled acrocyanosis; and that this spasm of vessels, designed to protect the body in general against the effects of hypothermia, may be so exaggerated that actual gangrene may occur even at normal temperatures. I think that we are justified in assuming that slight unrecognized degrees of hypothyroidism and hypothyrokinesis are likely to increase the liability to frostbite and immersion foot, as well as to other peripheral vascular disorders.

REFERENCES

BLOCK, W. (1944) *Bull. War Med.*, **4**, 268.
DIETRICH, S., and SCHWIEGK, H. (1932) *Arch. Exp. Path. Pharm.*, **165**, 53.
LEWIS, T., and LOVE, W. S. (1926) *Heart*, **13**, 27.
—— (1941) *Brit. med. J.* (ii), 837.
MADDOCK, W., and COLLER, F. A. (1933) *Am. J. Physiol.*, **106**, 589.
PICKERING, G. W., and HESS, W. (1933) *Clin. Sci.*, **1**, 213.
SHEARD, C., and WILLIAMS, M. M. D. (1940) *Proc. Mayo Clin.*, **15**, 758.

Professor J. R. Learmonth: *Arteriography in peripheral arterial disease.*—This paper deals with the value of arteriography in certain cases of peripheral vascular disease. Within the last few years I have been led to employ the method more frequently, not only for the precise information it gives for diagnosis and prognosis, but also in an endeavour to learn more about these distressing cases of young male patients with localized arterial thrombosis and with undoubted endarteritis obliterans.

Technique.—Unless I wished to study the behaviour of the arterial tree in cases suspected of showing undue sensitivity to exercise or to trauma, I have employed spinal anæsthesia in order that collateral vessels should be as widely dilated as possible. 120 mg. of novocain is given half an hour before the operation. The femoral artery is exposed, either immediately below Poupart's ligament in cases where one wishes to outline the profunda, or in Hunter's canal when it is suspected that the block is more distal. I believe it to be important that the artery should be disturbed as little as possible in its surroundings and I do not free it in its bed in any way. The opaque material used is perabrodil 50%, and 10 c.c. of this has proved to be enough for radiographic purposes. It is best to employ a syringe with an eccentric nozzle, and the needle (about No. 19) should have a long oblique bevel at its point in order that it may be introduced through the wall of the artery, bevel downwards, in a valvular manner. The injection of 10 c.c. of perabrodil occupies about five seconds, and the exposure is made while the last of the perabrodil is being injected. The picture has been made by a portable X-ray apparatus without a diaphragm, and I am indebted to Dr. Saffley and Mr. Grover for their help in this part of the work. On rare occasions local anæsthesia has been induced by infiltration with 2% novocain; when the artery has been exposed, it is important to soak its adventitial coat with local anæsthetic if the procedure is to be painless. There has not been any complication after arteriography; the small puncture in the wall of the artery closes itself in a few minutes under the gentle pressure of a moist swab.

The cases may be conveniently divided into certain groups:

Group I.—Localized Arterial Thrombosis

This condition has been considered in detail in a previous paper (Learmonth, J. R., Blackwood, W., and Richards, R. L., *Edin. Med. J.*, 1944, **51**, 1. It is a well-defined condition in which a thrombus forms in the lumen of one artery, the remaining vessels in the body being unaffected. It is readily identified in arteriograms by the normality of the arterial tree, with the exception of the part occupied by the thrombus which begins and ends "squarely".

cally demonstrable, the pituitary ceases its gonad-stimulating and thyroid-stimulating functions, and the patient develops amenorrhœa or impotence and an extreme degree of thyroxin deficiency which reduces the basal metabolic rate to the lowest figures ever found. Because the thyroid itself remains normal, it is inaccurate to speak of hypothyroidism. The failure is higher in the scale. The thyroid is no longer stimulated to activity by the pituitary and we should therefore speak rather of hypothyrokinesis.

My patient illustrates this well. Her hands and feet were deathly cold even in the hottest weather, but their temperature could be raised temporarily to normal by the prolonged use of a radiant heat cradle. Her basal metabolic rate (estimated by Dr. Douglas Robertson) was −48. That her condition was not due to hypothyroidism but to hypothyrokinesis is shown by fig. 1, which illustrates the effects of administering the thyroid-stimulating factor of the anterior pituitary.

FIG. 1.

A second patient, a girl of 15, was a case even more severe. Her basal metabolic rate was −51. All extremities, including her nose, were cold and blue. Her left hand was purplish red and stone cold to the touch

The skin of the forefinger was gangrenous, the pulp of the tip shrunken and the nail atrophied. There were small patches of shallow gangrene on all the fingers of the left hand. That this condition was due to arterial spasm was made clear by an ulnar and medial nerve block of the right (the better) hand. The temperature, on a very hot summer afternoon, was 71° F., and rose rapidly after nerve block to 88° F. That the spasm was due to low body temperature is made clear by the temperature and pulse charts. During treatment with thyrogan (fig. 2) great improvement occurred in the right hand,

FIG. 2.

FIG. 1.

FIG. 2.

FIG. 1 (*Case* 1).—Arteriogram showing the lower limit of the block in the femoral artery and the collateral circulation.
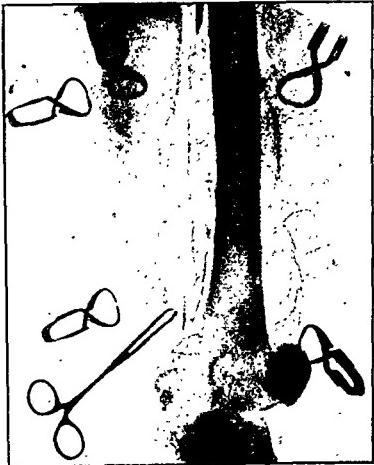
FIG. 2 (*Case* 1).—Arteriogram following resection of thrombosed segment. The site of the upper ligature is seen and also refilling of the popliteal artery.

FIG. 3.

FIG. 4.

FIG. 3 (*Case* 3).—Arteriogram showing high block of femoral artery and collateral circulation.

FIG. 4 (*Case* 9).—Arteriogram showing high block in femoral artery with very good collateral circulation.

Group III.—*Thrombo-angiitis Obliterans in Older Patients*

CASE VIII.—Male, aged 42. Claudication for one month in right leg. Right dorsalis pedis pulse absent, but posterior tibial present; both pulses present on left. In spite of the limitation of complaint to the right leg, reflex vasodilatation was almost equal in the great toes, the level reached being 31°C. The arteriogram shows a block in the femoral artery at the point where it passes through the adductor magnus muscle, with a collateral circulation which seems barely adequate to nourish the leg in spite of its freedom from nutritional disturbance. This patient was not operated on.

CASE IX.—Male, aged 42. Complaint of claudication in the left leg in which the posterior tibial pulse was just palpable. Reflex vasodilatation reached only 28° C. in the left great toe as compared with 32·5°C. in the right great toe. The arteriogram (fig. 4) shows a block high in the femoral artery with a considerable collateral circulation which was sufficient to delineate the vessels in the leg. This patient was not subjected to operation.

CASE I.—Aircraftman, aged 35. For one year paræsthesiæ in toes; later severe unilateral claudication followed by intractable ulcer on 5th toe. Peripheral pulses absent below the femoral. Reflex vasodilatation normal in the unaffected foot, absent in the other. The arteriogram (fig. 1) shows the distal end of the femoral artery refilled by the collateral circulation. Of special interest are the segment of the femoral artery forming a blind bay, and the origin of collaterals from the thrombosed segment. The affected length of artery was excised, and an arteriogram made after this operation (fig. 2) shows an adequate collateral circulation between the proximal end of the femoral artery and the popliteal artery. Two years after arteriectomy this patient remains in good health, and the ulcer has healed.

CASE II.—Male, aged 28. For four months stiffness in the right calf, with rapid shortening of claudication distance. No pulses below femoral. The block in the vessel is well shown in the arteriogram, and the state of the collateral circulation after lumbar sympathectomy in the second arteriogram. For a period of one and a half years the patient's claudication distance has gradually increased, and he returned to serve as a pilot in the Royal Air Force.

Group II.—Endarteritis Obliterans in Young Patients

In this group the block has been almost uniformly high in the femoral artery, usually at or about the point where the vessel passes through the adductor magnus to become the popliteal. In a number of cases there has been a history of trauma, but this does not seem to be of ætiological importance, although it may precipitate nutritional lesions in an area already deprived of part of its blood supply.

CASE III.—Male, aged 24. Gangrene of right great toe after an injury. The whole foot was grossly swollen and painful; efforts to reduce the œdema by elevation of the foot had to be discontinued, since in this position the pain was greatly intensified. The arteriogram (fig. 3) shows a block in the femoral artery at an unusual height, and disease of the branches of the profunda artery, which would otherwise have made a more substantial contribution to the circulation. This patient's leg was amputated above the knee. There were signs of the disease in the other limb, the posterior tibial pulse being absent although the dorsalis pedis pulse was present.

CASE IV.—Male, aged 30. While serving in the Near East in a very hot climate, this patient while lying in-bed felt his left foot go numb and observed that it was white. It can be taken that in so high an environmental temperature his peripheral vessels were dilated to their maximum, so that this event indicated a terminal blockage of collateral vessels which had previously been sufficient to provide an adequate circulation. In the opposite leg the posterior tibial pulse was present, but not the dorsalis pedis. The arteriogram shows a high block in the femoral artery with relatively poor collateral circulation. At this patient's own request, a lumbar sympathectomy was performed without any obvious benefit.

CASE V.—Male, aged 31. Four-year history of claudication in the right leg culminating in gangrene of the 3rd toe. An unsuccessful attempt to crush the peripheral nerves had been made elsewhere in order to provide relief from agonizing pain in the toe. In an attempt to save the limb, I first carried out chordotomy which relieved the pain, but after a short interval the gangrene spread rapidly. An arteriogram shows the femoral artery to be blocked at the point where it passes through the adductor magnus muscle, but the very adequate collateral circulation delineated encouraged me to carry out the inevitable amputation below the knee. The wound healed by first intention.

CASE VI.—Male, aged 32. Amputation of the left little toe had been performed elsewhere and the flaps had failed to heal. This had been treated by lumbar sympathectomy, and sweating tests showed that the intervention had been complete. The original arteriogram showed irregular narrowing of the femoral artery at one point. This area was explored in the hope that the patient had a localized lesion. At operation a short length of the artery was freed from its surroundings and from a tangle of veins which corresponded to the point of narrowing in the arteriogram. Above and below this point, as a result of handling, the artery went into spasm, a point of some interest in view of the previous sympathectomy and the spinal anæsthesia under which the operation was conducted. The arteriogram on the operating table shows the area in spasm quite clearly, and also collateral vessels refilling the popliteal artery. However, it is clear that the posterior tibial vessel is occluded although the anterior tibial artery remains patent. An absent posterior tibial pulse in the other limb showed that the disease was bilateral.

CASE VII.—Male, aged 36. This patient complained of aching pain in the foot brought on by exercise and relieved by rest. Later the pain was present even during rest, especially at night. In spite of the fact that it was impossible to palpate pulses in the other leg distal to the femoral, an arteriogram of the limb complained of shows patent femoral, popliteal and anterior and posterior tibial vessels. This patient belongs to the type in which the ultimate block is low in the posterior tibial vessel, a condition not infrequently associated with digital gangrene. In view of the acral distribution of the condition, a right lumbar sympathectomy was carried out with relief of pain and the promise of retention of the limb, at least for a time.

CASE XI.—Male, aged 39. While kneeling on a rifle range, this patient was accidentally shot by a machine gun, two bullets entering the left buttock and emerging anterior to the patella. Five months afterwards he complained of claudication in the calf and pain in the instep on exercise, and the dorsalis pedis and posterior tibial pulses were absent. Nutritional changes were present in the great and 2nd toes of the foot. Not unnaturally it had been surmised that the femoral vessels had been affected by the passage of the bullets and had become thrombosed. However the arteriogram shows multiple areas of narrowing of the main arterial trunks characteristic of thrombo-angiitis obliterans, the accidental wound being without ætiological importance in the production of the clinical picture.

Group IV.—? Arterial Sensitivity

In rare cases the arterial tree seems to be unusually sensitive to trauma and to exercise. The clinical picture is that of a middle-aged man who complains of claudication. On examination in bed under favourable conditions the pulses are present, but on exercise they disappear, or at least become exceedingly difficult to palpate. I have seen two patients of this type.

CASE XII.—Male, aged 32. Complaint of claudication. Pulses easily palpable on ordinary examination but becoming impalpable on exercise. An arteriogram was carried out under local anæsthesia, the object being first to make an arteriogram with the foot at rest, and subsequently to make an arteriogram after the foot had been exercised by pulling a weight up and down over a pulley. However, when the needle was entered into the artery, it at once went into spasm locally and the peripheral pulses disappeared. Perabrodil was injected and the arteriogram shows only a trickle of perabrodil reaching the posterior tibial artery which becomes extremely thin near the medial malleolus. In an endeavour to help this patient, a lumbar sympathectomy was performed on one side, and was proved complete by sweating tests. However, the condition persisted after this interruption of the extrinsic vasoconstrictor nerves to the limb, the distal pulses becoming impalpable after exercise as before. A year later this patient still suffers from claudication after exercise, the pulses still disappear, and the sympathectomized leg is no more useful than the other.

CASE XIII.—Male, aged 44. History of claudication for several months with disappearance of the peripheral pulses after exercise. The arteriogram was carried out under local anæsthesia, the posterior tibial pulse disappearing as in Case XII when the needle was inserted into the artery. The arteriogram (fig. 5) shows the posterior tibial vessel in a state of spasm and tapering off to become thread-like in its middle third. After this intervention the pulse returned in the posterior tibial vessel in thirty-five minutes.

Group V.—Syphilitic Disease

CASE XIV.—Male, aged 45. Three months' history of claudication with coldness and pallor of the feet, the left more affected than the right. Peripheral pulses absent on left side, present on right. Wassermann reaction strongly positive. The arteriogram (fig. 6) shows a block in the femoral artery at very much the same position as is seen in thrombo-angiitis obliterans, with the presence of collateral vessels which lack the tortuosity so characteristic of the active collaterals in at least the early stages of thrombo-angiitis obliterans.

Group VI.—History Indicative of Vascular Lesions without Clinical Findings

I have encountered more than one case in which the patient gave a history very characteristic of peripheral arterial insufficiency including claudication and coldness of the feet. In these cases clinical examination and arteriography failed to reveal any vascular lesion, and the patients were returned to duty.

CASE XV.—Male, aged 23. This patient was said to have had the femoral artery ligated for aneurysm while a prisoner of war in Germany. He gave a graphic story of claudication pain in the calf and coldness of the foot. However his vasomotor reactions were normal, and an arteriogram showed that the femoral artery had not been tied, but that a small branch of the medial circumflex artery had been interrupted in the neighbourhood of a metallic fragment.

CASE XVI.—Male, aged 22. This patient was said to have had the popliteal artery ligatured in the Middle East, and gave a history compatible with vascular insufficiency in the lower limb. Again, however, the vasomotor reactions were normal, and an arteriogram (fig. 7) showed that the popliteal artery was intact.

Group VII.—Absence of Peripheral Pulses, ? Vascular Insufficiency

CASE XVII.—Male, aged 37. This patient was admitted with a lesion of the lateral popliteal nerve resulting from a gunshot wound of the left tibia, and absent pulses in the left foot. With the lesion of Case XI still in my mind, it seemed to me possible that he was already suffering from thrombo-angiitis obliterans, and that the wound merely served to draw attention to the primary vascular condition. However, arteriography (fig. 8) showed that the arterial tree was intact, although the popliteal artery was somewhat narrowed in the region of the track of the bullet: nevertheless it provides an adequate circulation for both anterior and posterior tibial vessels. At the operation for suture of the lateral popliteal nerve, the popliteal artery was found to be pulsating normally throughout this part of its course.

FIG. 5.
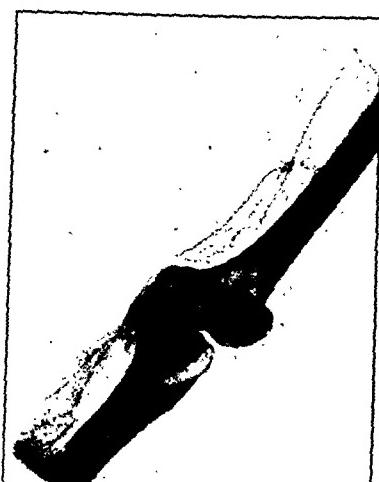
FIG. 6.

FIG. 5 (*Case* 13).—Arteriogram showing posterior tibial artery taperin towards its middle third.
FIG. 6 (*Case* 14).—Arteriogram showing femoral artery block in its lower third.

FIG. 7.

FIG. S.

FIG. 7 (*Case* 16).—Arteriogram showing patency of the popliteal artery after alleged ligation.
FIG. 8 (*Case* 17).—Arteriogram showing intact arterial tree with narrowing of the distal half of the popliteal artery.

CASE X.—Male, aged 43.   Sudden onset of pain in the right calf seven months before admission.   Two months before admission developed areas of superficial gangrene of the dry type over the leg and foot.   In the right leg pulses were not palpable distal to the femoral; all pulses were present on the left.   The arteriogram shows extraordinary narrowing of all the vessels in the arterial tree, with additional constrictions at the proximal part of the femoral vessel.   This curious case may possibly illustrate the occurrence of hypoplasia of the arterial tree of a limb, which, however, is adequate for nutrition until its total calibre is diminished by superimposed disease.   The limb was amputated above the knee, but the flaps were exceedingly slow to heal.

Mr. David H. Patey : The ordinary conception of thrombo-angiitis obliterans is of an obliterative vascular disease occurring in comparatively young men, with intermittent claudication as a characteristic and early symptom and clear-cut evidence of arterial obliteration on examination, as shown by absence of peripheral pulses, necrotic ulcers, gangrene and other similar gross signs. This picture, whilst only too typical of the advanced stages of the disease, gives a completely false impression of the early stages. It recalls the textbook descriptions of twenty years ago, when umbilicated nodules in the liver were given as one of the diagnostic signs of carcinoma of the stomach and papill-œdema as a cardinal point in the diagnosis of cerebral tumour. In fact, classical inter-mittent claudication so far from being an early symptom of thrombosis angiitis obliterans is more comparable to fæcal vomiting as a symptom of intestinal obstruction; it is an indication less of the existence of the disease than of its progress to the phase of irrever-sible complications. As a result, when a patient does present himself to a medical man in the real early stages of the disease, the correct diagnosis is almost invariably missed, even by the expert.

I have been particularly concerned with the study of the early symptoms and signs, and I would like to draw attention to an early symptom which I do not think has been clearly defined—what may be called "paradoxical response to exercise". For example, if a healthy man feeling a bit run down takes a golfing holiday, on the first day after a couple of rounds he may feel a bit tired and stiff but by the end of the holiday he takes his two rounds a day in his stride. But a similar man developing thrombo-angiitis obliterans finds that, whereas he starts off fairly all right with his two rounds a day, by the end of the week he finds himself only wanting to go out in the morning, and at the end of what would previously have been a rejuvenating holiday he finds himself ex-hausted and worn out. The earliest sign is differential cooling on exposure of the limbs, usually first seen in the feet. If under comparable conditions one limb becomes slightly, but definitely, cooler than its fellow and there is no obvious injury, disease or disuse of one limb to explain the difference, then this is very suggestive of organic vascular disease. I have found this early symptom and early sign present when the pulses at the wrist and ankle were apparently normal, the oscillometric response normal, when well-marked capillary pulsation was present in the fingers and toes, and the rate of reactive hyperæmia was within normal limits.

The causation of thrombo-angiitis obliterans is unknown, but I suggest we are more likely to find it in the early stages of the disease. The features of the later stages are unspecific in character and illustrate the effect of advanced arterial obstruction irre-spective of causation. It is impossible to be dogmatic, but I find difficulty in explaining all the early features of thrombo-angiitis obliterans on a purely vascular obstructive basis. In other words, there may be a prevascular syndrome, a point which, if it could be established, would be of great importance. Thrombo-angiitis obliterans in its early stages is probably an abnormality or deficiency in muscular metabolism, as a result of which an abnormal metabolite is formed which diffuses out both locally and into the circulation and has a deleterious action on the arteries.

Satisfactory treatment can only result from increased knowledge of causation. But even removal of the cause would not restore the position if irreversible changes had set in. And once damage of a certain degree has been done to the arteries spontaneous progression from thrombosis is likely even should the cause be satisfactorily dealt with. This emphasizes once more the importance of early diagnosis. Any new suggestions on treatment of a disease with such a variable and irregular course as thrombo-angiitis obliterans must be made with extreme caution, but I have felt that injections subcutan-eously once or twice a week of 25 mg. of vitamin B_1 for an indefinite period may be of value in the early stages of the disease.

Mr. Norman Lake said that he was in close agreement with almost everything that Professor Telford had said. The chief indication for operations upon the sympathetic system was peripheral vascular disease; in his series (much smaller than Professor Telford's) of over 200 cases no less than 160 operations had been performed for vascular disease and the results had been almost identical with those they had just heard recorded. He was especially interested in two aspects, one the extreme variations in the anatomy of the sympathetic system which had led Professor Telford to discard the usual method of describing the scope of sympathectomy by reference to numbered ganglia, and to adopt the plan of stating that portions of the chain within certain anatomical limits (i.e. vertebræ) were removed. This obviously has much to recommend it.

Professor J. Paterson Ross: *Ischæmic pain.*—"Intermittent limp, if the story could be dragged out of every patient, would probably be found to be the most common initial symptom of arteriosclerotic deficiency. . But among those who present themselves for the treatment of serious pain, ulceration, or actual gangrene it is not the usual presenting symptom." Thus wrote John Homans in his excellent monograph "Circulatory Diseases of the Extremities" (1939); and his statement makes it clear that there must be at least two distinct groups of symptoms to be distinguished in peripheral vascular disorders—the one which includes intermittent claudication, and the other which is premonitory of gangrene.

Our own investigations were interrupted by the war, but Boyd (1938) had already shown, by linking arteriographic studies to clinical manifestations, that the two groups of symptoms indicated disease at different levels in the arterial tree.

Intermittent claudication affecting the calf muscles is the symptom of blockage of the femoral or of the popliteal artery. It goes with postural colour changes in the foot, and with loss of the pulse in the popliteal artery and vessels distal to it, though it may happen infrequently, after the establishment of an unusually good collateral circulation, that a pulse again becomes perceptible at the ankle.

The level at which the popliteal artery is blocked is remarkably constant—just behind the condyles of the femur—though the upper part of the vessel is sometimes involved, leaving the lowest portion still patent. It is my impression that this variation in the level of the obstruction is important in prognosis, and in the response to sympathectomy. If the block is high in the popliteal artery or in the femoral the chance of re-establishing an adequate blood flow to the muscles of the calf is much better than if the popliteal artery is blocked at the level of the femoral condyles.

It is not generally recognized that a similar block of the posterior tibial artery can give rise to intermittent claudication in the muscles of the foot. Yet the collateral circulation under favourable conditions maintains a flow of blood through the plantar arches and digital vessels which is ample for the nutrition of the fore-foot and toes, and gangrene does not occur.

Intermittent claudication indicates obstruction of the proximal (main) arteries of the limb; and, since in a fair proportion of such cases the distal vessels remain healthy, there is no reason for gangrene to occur.

The pain which precedes or accompanies gangrene is entirely different. It is felt in the foot at rest, and is influenced by temperature and the posture of the limb, resembling in this respect the pain of acrocyanosis. The affected parts are discoloured, hyperæsthetic, and usually cold.

The best guide to the efficacy of any means of improving the peripheral circulation is its effect upon this "rest pain"; it may be relieved by conservative therapy, but if this fails, and particularly if the proximal pulses can be felt, sympathectomy offers the best hope of relief. If this fails major amputation is in my experience inevitable, though I would like to qualify that statement slightly so as to avoid any chance of misunderstanding.

It sometimes happens in the presence of gangrene that sympathectomy relieves the pain in the foot, though the gangrenous toe itself remains painful. In such cases, after waiting for the maximal improvement in the skin circulation, we have amputated the toe, taking special precautions against any avoidable injury to precariously nourished tissues, and with the healing of the wound all pain has vanished. On the other hand, the failure of this procedure is in itself good evidence of the necessity for a major amputation.

While there are easily recognizable differences between the pains produced by disease at different levels in the arterial tree, the clinical picture is incomplete if we omit the cases manifesting both kinds of pain, in which therefore we may infer that there is involvement of both the proximal and the distal vessels. Sometimes, as in senile arteriosclerosis, this is a diffuse change with gradual diminution in the calibre of the whole peripheral arterial tree. But there is another important disorder affecting younger men in which the popliteal artery is narrowed at the usual site behind the femoral condyles, and the digital arteries are also involved. Thrombosis occurs in them either as an incident in thrombo-angiitis obliterans or as a consequence of embolism by detached particles of mural clot from the diseased popliteal artery. It must be obvious that when both groups of symptoms and signs are thus combined the management of the case becomes extremely difficult, and the prognosis correspondingly more gloomy.

REFERENCE.
BOYD, A. M. (1938) *St. Bart's Hosp. Rep.*, 71, 151.

Section of Psychiatry

President—W. Norwood East, M.D., F.R.C.P.

[*June* 13, 1944]

Physical Constitution, Neurosis and Psychosis

By W. Linford Rees, M.D., B.Sc., M.R.C.P., D.P.M.

(*Mill Hill Emergency Hospital*)

Types of physique.—Body build has been variously classified since the recognition of a dichotomy of physique by Hippocrates, who describes the *habitus phthisicus,* a slender type, and its antithesis, the *habitus apoplecticus.* The classifications of Draper (1924) (gall-bladder and ulcer types), MacAuliffe (1925) (round and flat types), and Weidenreich (1926) (eurysome and leptosome) have continued to stress the dichotomy in body build. Rostan (1828) and the French school in general elaborated a tripartite scheme of body build (digestive, muscular, and respiratory-cerebral types) recently brought into favour by Kretschmer (1921) with his pyknic, athletic and asthenic types, and Sheldon (1940) with his endomorphic, mesomorphic and ectomorphic components of physique. Most classifications tend to describe two polar antithetical types of bodily architecture, some also including intermediate varieties.

New light on the subject of physical types has been shed by the recent use of the technique of Factorial Analysis in the field of body measurement. The method was first used by Burt (1938), Cohen (1938, 1940 and 1941), and later by Hammond (1942). The results suggested that the method might be useful:—

    (*a*) Determining the main types of body build;
    (*b*) Making it possible to derive an index of body build free from the arbitrariness with which many of the indices in the past had been constructed.

In collaboration with Dr. H. J. Eysenck, a factorial analysis was carried out on physical measurements taken on 200 successive soldiers admitted to Mill Hill Emergency Hospital. Age and seventeen measurements were intercorrelated and factorized by Burt's Summation Method. Two factors were abstracted which accounted for all the correlations within the limits of the probable error. The first factor contributed three times as much to the variance as the second factor and is a general factor influencing body size or growth in all directions. When the effect of this factor was removed, thus reducing individuals to the same general scale of size, a second factor became apparent. This factor was bipolar, having positive saturations with length measurements and negative saturations with breadth, depth and circumferential measurements. Thus when this factor expends itself predominantly in growth in length, there will be a relative deficiency of growth in breadth, width and circumference, and vice versa. This factor is therefore one of body type, dividing the narrow from the broad, corresponding to the polar antithetical types of other workers.

Stature and transverse chest diameter were the measurements having highest saturations with the opposite aspects of type factor and therefore most discriminative of physical

Sept.—Psych. 1

The second point was the reference to the application of sympathectomy to arterio-sclerosis. He agreed entirely that many of these cases gave gratifying results. That immediately raised the question of the value of the usual pre-operative tests. In his opinion they had been relied upon too implicitly—they might be roughly correct qualitatively but certainly not quantitatively. Following sympathectomy it is likely that a slow set of changes occur (parallel results are well seen in the bowel in Hirschsprung's disease) in addition to those which follow immediately upon withdrawal of sympathetic control, and it is clear that these cannot be estimated by any method of pre-operative test, whether carried out by spinal, regional or local injection, or by other means. On the whole the arteriosclerotic cases do not give a very satisfactory response to pre-operative tests and yet, as Professor Telford has shown, the delayed post-operative results were often good.

Professor Telford had said that the lumbar sympathetic chain contained no afferent fibres, but was it not usually accepted that pain impulses from the vessels (possibly arising from the muscular coat) travelled by this route? Like Professor Learmonth he had seen vessels go into tight spasm during arteriography; was this due to the mechanical stimulation of the needle or to the chemical nature of the injection?

Mr. A. Dickson Wright said that the use of ganglionectomy in chronic disease had been well worked out by Professor Telford but he felt that sufficient attention had not been paid to the value of sympathetic surgery in vascular emergencies. Leriche's technique of infiltrating the lumbar ganglia with novocain in phlegmasia alba dolens gave such remarkable results that it was strange that its adoption in this country was so slow.

If sympathectomy was done in association with ligature of the large arteries and in cases of traumatic arterial spasm, injuries to arteries and embolism of arteries then there would be a great reduction in the number of amputations required.

Professor Learmonth (replying to Mr. Norman Lake) said he considered the spasm was due to the mechanical stimulation of the needle, since he had seen it occur before the injection was begun. For the material used, see under "Technique"—perabrodil 50%.

Professor Telford (also in reply) said that as the result of observations made by Professor Stopford and himself and after studying the experimental work of Professor Waterston he was of opinion that the relief of pain after sympathectomy was due to the improvement in the circulation rather than to any section of afferent fibres.

Section of Psychiatry

President—W. Norwood East, M.D., F.R.C.P.

[*June* 13, 1944]

Physical Constitution, Neurosis and Psychosis

By W. Linford Rees, M.D., B.Sc., M.R.C.P., D.P.M.

(*Mill Hill Emergency Hospital*)

Types of physique.—Body build has been variously classified since the recognition of a dichotomy of physique by Hippocrates, who describes the *habitus phthisicus*, a slender type, and its antithesis, the *habitus apoplecticus*. The classifications of Draper (1924) (gall-bladder and ulcer types), MacAuliffe (1925) (round and flat types), and Weidenreich (1926) (eurysome and leptosome) have continued to stress the dichotomy in body build. Rostan (1828) and the French school in general elaborated a tripartite scheme of body build (digestive, muscular, and respiratory-cerebral types) recently brought into favour by Kretschmer (1921) with his pyknic, athletic and asthenic types, and Sheldon (1940) with his endomorphic, mesomorphic and ectomorphic components of physique. Most classifications tend to describe two polar antithetical types of bodily architecture, some also including intermediate varieties.

New light on the subject of physical types has been shed by the recent use of the technique of Factorial Analysis in the field of body measurement. The method was first used by Burt (1938), Cohen (1938, 1940 and 1941), and later by Hammond (1942). The results suggested that the method might be useful:—

    (a) Determining the main types of body build;

    (b) Making it possible to derive an index of body build free from the arbitrariness with which many of the indices in the past had been constructed.

In collaboration with Dr. H. J. Eysenck, a factorial analysis was carried out on physical measurements taken on 200 successive soldiers admitted to Mill Hill Emergency Hospital. Age and seventeen measurements were intercorrelated and factorized by Burt's Summation Method. Two factors were abstracted which accounted for all the correlations within the limits of the probable error. The first factor contributed three times as much to the variance as the second factor and is a general factor influencing body size or growth in all directions. When the effect of this factor was removed, thus reducing individuals to the same general scale of size, a second factor became apparent. This factor was bipolar, having positive saturations with length measurements and negative saturations with breadth, depth and circumferential measurements. Thus when this factor expends itself predominantly in growth in length, there will be a relative deficiency of growth in breadth, width and circumference, and vice versa. This factor is therefore one of body type, dividing the narrow from the broad, corresponding to the polar antithetical types of other workers.

Stature and transverse chest diameter were the measurements having highest saturations with the opposite aspects of type factor and therefore most discriminative of physical

Sept.—Psych. 1

types. As both measurements have similar saturations with the general factor, dividing one measurement by the other will eliminate the effect of body size, while the size of the fraction will indicate the position of the subject on the body type continuum. The index

$$\frac{\text{Stature} \times 100}{6 \times \text{Transverse Chest Diameter}}$$

was therefore used for objectively discriminating physical types. Transverse chest diameter is multiplied by 6, as stature on the average is 6 times as large as this measurement, and multiplying by 100 will tend to give a mean value near 100, with the group dispersed around this convenient central value.

The index was taken on 400 neurotic soldiers successively admitted to Mill Hill Emergency Hospital. The frequency distribution curve was found to be normal in type, there was no evidence of bimodality, and therefore no evidence of discrete types except in so far as they are regarded as extremes of the normal distribution. While no evidence for definitely segregated physical types of the kind envisaged by Kretschmer (1921) was found, it will be helpful to divide the group into three types on the basis of the frequency distribution curve. We propose to call those individuals whose index of body type is more than 1 S.D. above the Mean "Leptomorphs", those whose index is within 1 S.D. either way of the Mean "Mesomorphs", and those whose index value is more than 1 S.D. below the Mean "Eurymorphs". We do not wish to imply lack of continuity between the three groups and have only separated them out in this way for the sake of convenience, using arbitrary dividing points.

Physique and effort syndrome.—An anthropometric investigation was carried out on 200 soldiers suffering from effort syndrome, with the primary purpose of determining whether effort syndrome patients as a group differed significantly in body build from the normal, and secondarily to determine the relationship between type of physique and the development and form of the syndrome. Seventeen absolute measurements were taken on the effort syndrome group and also on a control group of 100 normal soldiers of similar age distribution and military status. The significance of the differences in the measurements was determined by the critical ratio. The effort syndrome group was found to be significantly greater in certain length measurements (stature, suprasternal height and trunk length) and significantly smaller in breadth and width measurements (shoulder breadth, breadth and depth of chest), indicating a narrower or more leptomorphic type of body build than the normal. This conclusion was confirmed by significant difference in the index of body type and Strömgren index. From the index values the following distribution of physical types was found in the effort syndrome group:—

Leptomorphs 50%.   Mesomorphs 44%.   Eurymorphs 6%.

The corresponding distribution in the normal group was:—

Leptomorphs 21%.   Mesomorphs 58%.   Eurymorphs 21%.

The effort syndrome group has a significantly greater percentage of leptomorphs and a significantly smaller percentage of eurymorphs. These findings point a significant association between effort syndrome and the leptomorphic type of body build and suggest that leptomorphic habitus may be a factor in the development of the syndrome.

On comparing the case records of the group of leptomorphic effort syndrome patients with those of eurymorphic physique, striking differences were found.

85% of the leptomorphs had a history of effort intolerance and vegetative disequilibrium from an early age, compared with only 7% in the eurymorphic group. The leptomorphic group showed a higher incidence of (1) unsatisfactory factors in the family history, (2) life-long timidity, anxiety symptoms and general neuroticism, (3) chronic hypochondriasis. The eurymorphs, on the other hand, were characterized by a comparatively short duration of illness, which tended to be brought on by exogenous factors, such as febrile illness or marked environmental stress (e.g. severe enemy action).

Thus in leptomorphic patients endogenous or constitutional factors predominate in the ætiology, whereas in the eurymorphic effort syndrome patients constitutional factors play a less important role than exogenous factors in the causation of the syndrome.

Physical constitution and neurosis.—Physical measurements were carried out on 389 soldiers who were successive admissions to Mill Hill Emergency Hospital, with a view to determining the relationship between physique, temperament, and neurosis. The index of body type was calculated for this group and compared with that of 100 normal

soldiers of similar age distribution and military status. The Means showed no significant difference, but the standard deviation for the neurotic group was significantly greater than that of the normal group, indicating that the neurotic population contained more extreme types of body build than the normal. The experimental population of 389 soldiers was divided into three groups by means of the index of body build, as described in the previous section, giving 60 leptomorphs, 241 mesomorphs, and 88 eurymorphs. The group of 389 soldiers had been rated by the psychiatrist in charge on some 200 points relating to family and personal history, personality diagnosis, &c. The frequency of each item was found for the three groups and the significance of the differences tested by means of the critical ratio.

Briefly, the results indicated that leptomorphs tended to have psychasthenic symptoms (anxiety, depression and obsessional symptoms) and eurymorphs hysterical symptoms. Leptomorphs showed a greater incidence of schizoid traits than mesomorphs and eurymorphs. Mesomorphs tended to be intermediate between eurymorphs and leptomorphs in the majority of traits examined, just as they are intermediate in body build. On the whole, the data are presented not as final proof, but as evidence both confirmatory and suggestive of complex relations between body type, personality and neurosis.

Physique and psychosis.—An anthropometric investigation was carried out on a group of 42 manic depressives and a group of 49 schizophrenics. Seventeen absolute measurements were taken on both groups and various indices of body build calculated.

Both groups were significantly smaller in stature than the normal group, and significant differences in body build indices showed that the manic depressive group was more eurymorphic and the schizophrenic group more leptomorphic than the normal group.

The manic depressive group was smaller than the schizophrenic group in length measurements, but not statistically significantly so.

The manic depressive group was significantly greater than the schizophrenic in certain breadth, depth and circumferential measurements. Sagittal chest diameter showed the most significant difference (critical ratio $= 6 \cdot 18$) and next bicristal diameter (critical ratio $= 2 \cdot 48$) and hip circumference (critical ratio $= 2 \cdot 47$).

The most discriminative index was that of Strömgren (1937) which includes sagittal chest diameter.

The results showed that the manic depressive group is significantly more eurymorphic than the schizophrenic group. The distribution of physical types as shown by Strömgren's index was, in manic depressive group, leptomorph 9%, mesomorph 58%, eurymorph 33%; in schizophrenic group, leptomorph 34%, mesomorph 46%, and eurymorph 20%. The results on the whole support Kretschmer's theory. The percentage of eurymorphs in the schizophrenic group, however, is higher than indicated in Kretschmer's theory. In this connexion it is interesting to note that Connolly (1939) found that paranoid schizophrenics tended to be of pyknic habitus.

The age difference between the two groups is great. The Mean age of the schizophrenic group was 28·7 years, S.D. 11·67, and that of the manic depressive group 50·4 years, S.D. 13·43. The question whether the age factor accounts for our results is a pertinent one, as both manic depressive psychosis and the eurymorphic habitus tend to occur in greater frequency in the older age groups, and it seems possible that the association could be due to this temporal coincidence. The group was too small for extensive partitioning into age-groups. Excluding patients older than 45 years, there were 15 patients with a mean age of 35·4. This group still had a higher percentage of eurymorphs than the normal group, and as a group as a whole was more eurymorphic. The older age-groups of manic depressives did, however, show a higher frequency of eurymorphs than the younger age-groups. Age was found to have a correlation of $-\cdot236$ with the type factor in a group of 200 soldiers, indicating only a slight tendency for individuals of older age-groups to be more eurymorphic in physique. On the data available we conclude that the age factor may account for a part of the association between manic depressive psychosis and the eurymorphic habitus, but is considered unlikely to play such a strong part as to invalidate the Kretschmerian theory.

Type of physique and prognosis.—The question of the possible effect that type of body build may have in determining the clinical picture and the outcome of psychotic illness has as yet received little attention. The available results, however, are both interesting and suggestive.

Mauz (1930) found that the pyknic physique influences against a catastrophic course and favours remissions in schizophrenia.

types. As both measurements have similar saturations with the general factor, dividing one measurement by the other will eliminate the effect of body size, while the size of the fraction will indicate the position of the subject on the body type continuum. The index

$$\frac{\text{Stature} \times 100}{6 \times \text{Transverse Chest Diameter}}$$

was therefore used for objectively discriminating physical types. Transverse chest diameter is multiplied by 6, as stature on the average is 6 times as large as this measurement, and multiplying by 100 will tend to give a mean value near 100, with the group dispersed around this convenient central value.

The index was taken on 400 neurotic soldiers successively *admitted to* Mill Hill Emergency Hospital. The frequency distribution curve was found to be normal in type, there was no evidence of bimodality, and therefore no evidence of discrete types except in so far as they are regarded as extremes of the normal distribution. While no evidence for definitely segregated physical types of the kind envisaged by Kretschmer (1921) was found, it will be helpful to divide the group into three types on the basis of the frequency distribution curve. We propose to call those individuals whose index of body type is more than 1 S.D. above the Mean "Leptomorphs", those whose index is within 1 S.D. either way of the Mean "Mesomorphs", and those whose index value is more than 1 S.D. below the Mean "Eurymorphs". We do not wish to imply lack of continuity between the three groups and have only separated them out in this way for the sake of convenience, using arbitrary dividing points.

Physique and effort syndrome.—An anthropometric investigation was carried out on 200 soldiers suffering from effort syndrome, with the primary purpose of determining whether effort syndrome patients as a group differed significantly in body build from the normal, and secondarily to determine the relationship between type of physique and the development and form of the syndrome. Seventeen absolute measurements were taken on the effort syndrome group and also on a control group of 100 normal soldiers of similar age distribution and military status. The significance of the differences in the measurements was determined by the critical ratio. The effort syndrome group was found to be significantly greater in certain length measurements (stature, suprasternal height and trunk length) and significantly smaller in breadth and width measurements (shoulder breadth, breadth and depth of chest), indicating a narrower or more leptomorphic type of body build than the normal. This conclusion was confirmed by significant difference in the index of body type and Strömgren index. From the index values the following distribution of physical types was found in the effort syndrome group:—

        Leptomorphs 50%.   Mesomorphs 44%.   Eurymorphs 6%.

The corresponding distribution in the normal group was:—

        Leptomorphs 21%.   Mesomorphs 58%.   Eurymorphs 21%.

The effort syndrome group has a significantly greater percentage of leptomorphs and a significantly smaller percentage of eurymorphs. These findings point a significant association between effort syndrome and the leptomorphic type of body build and suggest that leptomorphic habitus may be a factor in the development of the syndrome.

On comparing the case records of the group of leptomorphic effort syndrome patients with those of eurymorphic physique, striking differences were found.

85% of the leptomorphs had a history of effort intolerance and vegetative disequilibrium from an early age, compared with only 7% in the eurymorphic group. The leptomorphic group showed a higher incidence of (1) unsatisfactory factors in the family history, (2) life-long timidity, anxiety symptoms and general neuroticism, (3) chronic hypochondriasis. The eurymorphs, on the other hand, were characterized by a comparatively short duration of illness, which tended to be brought on by exogenous factors, such as febrile illness or marked environmental stress (e.g. severe enemy action).

Thus in leptomorphic patients endogenous or constitutional factors predominate in the ætiology, whereas in the eurymorphic effort syndrome patients constitutional factors play a less important role than exogenous factors in the causation of the syndrome.

Physical constitution and neurosis.—Physical measurements were carried out on 389 soldiers who were successive admissions to Mill Hill Emergency Hospital, with a view to determining the relationship between physique, temperament, and neurosis. The index of body type was calculated for this group and compared with that of 100 normal

soldiers of similar age distribution and military status. The Means showed no significant difference, but the standard deviation for the neurotic group was significantly greater than that of the normal group, indicating that the neurotic population contained more extreme types of body build than the normal. The experimental population of 389 soldiers was divided into three groups by means of the index of body build, as described in the previous section, giving 60 leptomorphs, 241 mesomorphs, and 88 eurymorphs. The group of 389 soldiers had been rated by the psychiatrist in charge on some 200 points relating to family and personal history, personality diagnosis, &c. The frequency of each item was found for the three groups and the significance of the differences tested by means of the critical ratio.

Briefly, the results indicated that leptomorphs tended to have psychasthenic symptoms (anxiety, depression and obsessional symptoms) and eurymorphs hysterical symptoms. Leptomorphs showed a greater incidence of schizoid traits than mesomorphs and eurymorphs. Mesomorphs tended to be intermediate between eurymorphs and leptomorphs in the majority of traits examined, just as they are intermediate in body build. On the whole, the data are presented not as final proof, but as evidence both confirmatory and suggestive of complex relations between body type, personality and neurosis.

Physique and psychosis.—An anthropometric investigation was carried out on a group of 42 manic depressives and a group of 49 schizophrenics. Seventeen absolute measurements were taken on both groups and various indices of body build calculated.

Both groups were significantly smaller in stature than the normal group, and significant differences in body build indices showed that the manic depressive group was more eurymorphic and the schizophrenic group more leptomorphic than the normal group.

The manic depressive group was smaller than the schizophrenic group in length measurements, but not statistically significantly so.

The manic depressive group was significantly greater than the schizophrenic in certain breadth, depth and circumferential measurements. Sagittal chest diameter showed the most significant difference (critical ratio = 6·18) and next bicristal diameter (critical ratio = 2·48) and hip circumference (critical ratio = 2·47).

The most discriminative index was that of Strömgren (1937) which includes sagittal chest diameter.

The results showed that the manic depressive group is significantly more eurymorphic than the schizophrenic group. The distribution of physical types as shown by Strömgren's index was, in manic depressive group, leptomorph 9%, mesomorph 58%, eurymorph 33%; in schizophrenic group, leptomorph 34%, mesomorph 46%, and eurymorph 20%. The results on the whole support Kretschmer's theory. The percentage of eurymorphs in the schizophrenic group, however, is higher than indicated in Kretschmer's theory. In this connexion it is interesting to note that Connolly (1939) found that paranoid schizophrenics tended to be of pyknic habitus.

The age difference between the two groups is great. The Mean age of the schizophrenic group was 28·7 years, S.D. 11·67, and that of the manic depressive group 50·4 years, S.D. 13·43. The question whether the age factor accounts for our results is a pertinent one, as both manic depressive psychosis and the eurymorphic habitus tend to occur in greater frequency in the older age groups, and it seems possible that the association could be due to this temporal coincidence. The group was too small for extensive partitioning into age-groups. Excluding patients older than 45 years, there were 15 patients with a mean age of 35·4. This group still had a higher percentage of eurymorphs than the normal group, and as a group as a whole was more eurymorphic. The older age-groups of manic depressives did, however, show a higher frequency of eurymorphs than the younger age-groups. Age was found to have a correlation of −·236 with the type factor in a group of 200 soldiers, indicating only a slight tendency for individuals of older age-groups to be more eurymorphic in physique. On the data available we conclude that the age factor may account for a part of the association between manic depressive psychosis and the eurymorphic habitus, but is considered unlikely to play such a strong part as to invalidate the Kretschmerian theory.

Type of physique and prognosis.—The question of the possible effect that type of body build may have in determining the clinical picture and the outcome of psychotic illness has as yet received little attention. The available results, however, are both interesting and suggestive.

Mauz (1930) found that the pyknic physique influences against a catastrophic course and favours remissions in schizophrenia.

types. As both measurements have similar saturations with the general factor, dividing one measurement by the other will eliminate the effect of body size, while the size of the fraction will indicate the position of the subject on the body type continuum. The index

$$\frac{\text{Stature} \times 100}{6 \times \text{Transverse Chest Diameter}}$$

was therefore used for objectively discriminating physical types. Transverse chest diameter is multiplied by 6, as stature on the average is 6 times as large as this measurement, and multiplying by 100 will tend to give a mean value near 100, with the group dispersed around this convenient central value.

The index was taken on 400 neurotic soldiers successively admitted to Mill Hill Emergency Hospital. The frequency distribution curve was found to be normal in type, there was no evidence of bimodality, and therefore no evidence of discrete types except in so far as they are regarded as extremes of the normal distribution. While no evidence for definitely segregated physical types of the kind envisaged by Kretschmer (1921) was found, it will be helpful to divide the group into three types on the basis of the frequency distribution curve. We propose to call those individuals whose index of body type is more than 1 S.D. above the Mean "Leptomorphs", those whose index is within 1 S.D. either way of the Mean "Mesomorphs", and those whose index value is more than 1 S.D. below the Mean "Eurymorphs". We do not wish to imply lack of continuity between the three groups and have only separated them out in this way for the sake of convenience, using arbitrary dividing points.

Physique and effort syndrome.—An anthropometric investigation was carried out on 200 soldiers suffering from effort syndrome, with the primary purpose of determining whether effort syndrome patients as a group differed significantly in body build from the normal, and secondarily to determine the relationship between type of physique and the development and form of the syndrome. Seventeen absolute measurements were taken on the effort syndrome group and also on a control group of 100 normal soldiers of similar age distribution and military status. The significance of the differences in the measurements was determined by the critical ratio. The effort syndrome group was found to be significantly greater in certain length measurements (stature, suprasternal height and trunk length) and significantly smaller in breadth and width measurements (shoulder breadth, breadth and depth of chest), indicating a narrower or more leptomorphic type of body build than the normal. This conclusion was confirmed by significant difference in the index of body type and Strömgren index. From the index values the following distribution of physical types was found in the effort syndrome group:—

Leptomorphs 50%.   Mesomorphs 44%.   Eurymorphs 6%.

The corresponding distribution in the normal group was:—

Leptomorphs 21%.   Mesomorphs 58%.   Eurymorphs 21%.

The effort syndrome group has a significantly greater percentage of leptomorphs and a significantly smaller percentage of eurymorphs. These findings point a significant association between effort syndrome and the leptomorphic type of body build and suggest that leptomorphic habitus may be a factor in the development of the syndrome.

On comparing the case records of the group of leptomorphic effort syndrome patients with those of eurymorphic physique, striking differences were found.

85% of the leptomorphs had a history of effort intolerance and vegetative disequilibrium from an early age, compared with only 7% in the eurymorphic group. The leptomorphic group showed a higher incidence of (1) unsatisfactory factors in the family history, (2) life-long timidity, anxiety symptoms and general neuroticism, (3) chronic hypochondriasis. The eurymorphs, on the other hand, were characterized by a comparatively short duration of illness, which tended to be brought on by exogenous factors, such as febrile illness or marked environmental stress (e.g. severe enemy action).

Thus in leptomorphic patients endogenous or constitutional factors predominate in the aetiology, whereas in the eurymorphic effort syndrome patients constitutional factors play a less important role than exogenous factors in the causation of the syndrome.

Physical constitution and neurosis.—Physical measurements were carried out on 389 soldiers who were successive admissions to Mill Hill Emergency Hospital, with a view to determining the relationship between physique, temperament, and neurosis. The index of body type was calculated for this group and compared with that of 100 normal

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*April* 20, 1944]

Lupoid "rosaceous" Tuberculide.—ROBERT KLABER, M.D.

Woman aged 34; for seven years has had persistent guttate lesions on both cheeks, backs of arms, and backs of hands. On the cheeks they are scarcely raised above the surface and show a yellow lupoid centre surrounded by a rosaceous halo, most marked on the lower part of both cheeks. More numerous, though mostly smaller, similar lesions are present on the backs of the forearms and backs of the hands. A few new ones have recently appeared on the backs of the lower half of the legs, but the other areas have remained virtually unchanged since they first appeared, in spite of treatment with general ultra-violet light, gold, iodine, and arsenic. Her general health is good, as it has always been, although she gets easily tired.

Family history.—Her mother's sister and her step-father both died of pulmonary tuberculosis, and her step-brother who used to live with her as a child, also has pulmonary tuberculosis.

Two months ago, without any evident septic focus, an enlarged painless gland appeared in the left axilla, but has since disappeared. Mantoux reaction is negative to 1:1,000 dilution O.T. Wassermann reaction is negative. X-rays of chest and hands show no evidence of tuberculosis or sarcoid. Histology of row of nodules shows parcels of epithelioid cells with lymphocytic sheath rather like a sarcoid type of reaction. The extensive central necrosis in the largest lesions is more suggestive of a tuberculide.

Dr. Louis Forman: I did not agree with the diagnosis because of the absence of rosacea, either active or passive, and the absence of the translucent yellow colour of a granuloma on compression. I would regard it as a tuberculide rather than a sarcoid.

Dr. J. E. M. Wigley: At a meeting some years ago there was a good deal of discussion on rosaceous tuberculide, and I seem to remember that Dr. MacLeod rather deprecated this multiplication of names for conditions which were essentially the same. I think he would have recognized this as papulo-necrotic tuberculide occurring on certain parts of the body and left it at that.

Dr. H. C. Semon: These cases sometimes respond to a strict salt-free diet. In a case which I am showing this afternoon that was the only line of treatment which appeared to do any good. A salt-free diet with general light baths might be worth trying in this case.

Dr. Robert Klaber: All the lesions were markedly congestive. Those on the arms and lower legs without glass pressure show no yellow centre at all; they are simply deep red macules. If the term "rosaceous" is to be used at all, it is as aptly descriptive of this case as any other.

With regard to the multiplicity of other titles, I think that papulo-necrotic tuberculides are of a much more active type and that this patient's lesions, both in their appearance and course, are quite distinct. In fact, they are scarcely even papular. I should be more than happy to withdraw the adjective "rosaceous" and leave the diagnosis as "lupoid tuberculide".

Dr. Wigley: Is not that a contradiction in terms

Dr. Klaber: No. It means a lupus-like tuberculide. The alternative would be "lupus miliaris faciei disseminata". This, however, usually occurs only on the face. It should not, I think, be called lupus.

Dr. S. F. Bruenauer: Cases are described in the literature as lupus miliaris involving the face only, but others in the older literature show the same condition developing on the upper limb too. I should call Dr. Klaber's case lupus miliaris involving the upper limb.

The President: You would not call it strictly lupus.

Dr. Bruenauer: Histologically I should say there is a definite resemblance.

SEPT.—DERMAT. 1

Kisselew (1931) found that schizophrenics of pyknic physique showed better rapport and less scattered thinking than those of asthenic physique.

Plattner-Heberlein (1932) showed that pyknic schizophrenics tended to preserve affective relations with the environment.

Betz (1942) found that schizophrenic women of asthenic habitus show a greater degree of defect in mental status and a more frequent deterioration in course. Pyknics, on the other hand, tend to have a higher frequency of hallucinations and delusions, an older age of onset, and a lesser tendency to deterioration.

The results, therefore, show that the physical aspect of human constitution is more than an incidental factor, not only in determining susceptibility to psychosis, but also influencing the form and progress of the illness. The study of physical constitution as an integral part of the total personality should prove an interesting subject for further clinical research in psychiatry.

REFERENCES

BETZ, B. J. (1942) *Hum. Biol.*, **14**, 192.
BURT, C. (1938) *Brit. J. med. Psychol.*, **17**, 184.
COHEN, J. I. (1938) *J. ment. Sci.*, **84**, 495.
—— (1940) *J. ment. Sci.*, **86**, 602.
—— (1941) *Brit. J. med. Psychol.*, **18**, 323.
CONNOLLY, C. J. (1939) *Stud. Psychol. Psychiat. Cathol. Univ. Amer.*, **4**, No. 5.
DRAPER, G. (1924) Human Constitution. Philadelphia.
HAMMOND, W. H. (1942) *Man*, **42**, 4.
KISSELEW, M. W. (1931) *Z. ges. Neurol. Psychiat.*, **132**, 18.
KRETSCHMER, E. (1921) Körperbau u. Charakter. Berlin.
MACAULIFFE, L. (1925) *Bull. Soc. d'Étude des Formes Humaines*, Nos. 2 and 3, 155.
MAUZ, F. (1930) Die Prognostik der endogenen Psychosen. Leipzig.
PLATTNER-HEBERLEIN, F. (1932) *Z. ges. Neurol. Psychiat.*, **141**, 277.
ROSTAN, L. (1828) Cours élémentaire d'hygiène. Paris.
SHELDON, W. H. (1940) Varieties of Human Physique. New York and London.
STRÖMGREN, E. (1937) *Z. ges. Neurol. Psychiat.*, **159**, 75.
WEIDENREICH, F. (1926) Rasse und Körperbau. Berlin.

Section of Dermatology

President—A. C. ROXBURGH, M.D.

[*April 20, 1944*]

Lupoid "rosaceous" Tuberculide.—ROBERT KLABER, M.D.

Woman aged 34; for seven years has had persistent guttate lesions on both cheeks, backs of arms, and backs of hands. On the cheeks they are scarcely raised above the surface and show a yellow lupoid centre surrounded by a rosaceous halo, most marked on the lower part of both cheeks. More numerous, though mostly smaller, similar lesions are present on the backs of the forearms and backs of the hands. A few new ones have recently appeared on the backs of the lower half of the legs, but the other areas have remained virtually unchanged since they first appeared, in spite of treatment with general ultra-violet light, gold, iodine, and arsenic. Her general health is good, as it has always been, although she gets easily tired.

Family history.—Her mother's sister and her step-father both died of pulmonary tuberculosis, and her step-brother who used to live with her as a child, also has pulmonary tuberculosis.

Two months ago, without any evident septic focus, an enlarged painless gland appeared in the left axilla, but has since disappeared. Mantoux reaction is negative to 1:1,000 dilution O.T. Wassermann reaction is negative. X-rays of chest and hands show no evidence of tuberculosis or sarcoid. Histology of row of nodules shows parcels of epithelioid cells with lymphocytic sheath rather like a sarcoid type of reaction. The extensive central necrosis in the largest lesions is more suggestive of a tuberculide.

Dr. Louis Forman: I did not agree with the diagnosis because of the absence of rosacea, either active or passive, and the absence of the translucent yellow colour of a granuloma on compression. I would regard it as a tuberculide rather than a sarcoid.

Dr. J. E. M. Wigley: At a meeting some years ago there was a good deal of discussion on rosaceous tuberculide, and I seem to remember that Dr. MacLeod rather deprecated this multiplication of names for conditions which were essentially the same. I think he would have recognized this as papulo-necrotic tuberculide occurring on certain parts of the body and left it at that.

Dr. H. C. Semon: These cases sometimes respond to a strict salt-free diet. In a case which I am showing this afternoon that was the only line of treatment which appeared to do any good. A salt-free diet with general light baths might be worth trying in this case.

Dr. Robert Klaber: All the lesions were markedly congestive. Those on the arms and lower legs without glass pressure show no yellow centre at all; they are simply deep red macules. If the term "rosaceous" is to be used at all, it is as aptly descriptive of this case as any other.

With regard to the multiplicity of other titles, I think that papulo-necrotic tuberculides are of a much more active type and that this patient's lesions, both in their appearance and course, are quite distinct. In fact, they are scarcely even papular. I should be more than happy to withdraw the adjective "rosaceous" and leave the diagnosis as "lupoid tuberculide".

Dr. Wigley: Is not that a contradiction in terms

Dr. Klaber: No. It means a lupus-like tuberculide. The alternative would be "lupus miliaris faciei disseminata". This, however, usually occurs only on the face. It should not, I think, be called lupus.

Dr. S. F. Bruenauer: Cases are described in the literature as lupus miliaris involving the face only, but others in the older literature show the same condition developing on the upper limb too. I should call Dr. Klaber's case lupus miliaris involving the upper limb.

The President: You would not call it strictly lupus.

Dr. Bruenauer: Histologically I should say there is a definite resemblance.

Naevus Cutis Verticis Gyratus.—ROBERT KLABER, M.D.

Fishmonger aged 43. The condition on the scalp has not materially altered since its appearance at birth. He has been able for years to carry fish-boxes upon his head without any discomfort. The scalp shows from seven to ten well marked "convolutions" covering the greater part of the left side of the scalp, from which it extends a little over the midline (fig. 1). The occiput shows a large lobed fleshy naevus with several blue areas suggesting deep pigmentation (fig. 2). The frontotemporal margin of the main convoluted

FIG. 1.   FIG. 2.

Nævus cutis verticis gyratus.

area shows a fairly deep pigmentation. These facts, together with the presence of large numbers of pigmented moles on the trunk and lower limbs, suggest that the "convolutions" also result from a naevus.

Dr. F. Parkes Weber: If Dr. Klaber had simply entitled this case "cutis verticis gyrata" there might have been some discussion, but as he has called it a "nævus gyratus" of the skin of the top of the head there can be no difference of opinion, because he has thereby truly described the whole condition together with its nature. The differential diagnosis from acromegalic and other forms of cutis verticis gyrata might have been discussed, but he has precluded that by calling the condition a "nævus gyratus," and everybody is agreed that this type of cutis gyrata is a nævus.

Erythema Annulare Centrifugum (Darier).—ROBERT KLABER, M.D.

Girl aged 18, in good general health. She has a three weeks' history only, of multiple centrifugal rings on cheeks and forehead, only very slightly raised and pink. There is slight irritation and increased redness in the evenings. No visible scaling, teeth and tonsils show no gross sepsis, and there are no signs of any epidermophytosis which Sutton and Sutton found in three of their cases. Sinuses not yet investigated.

The President: There were very faintly marked rings on the forehead and cheeks. I do not know what else it could be if not erythema annulare centrifugum. She said that the lesions did enlarge.

Asphyxia Reticularis Multiplex (Unna).—G. ALLAN YORKE, M.R.C.S., L.R.C.P. (for Dr. ROBERT KLABER).

Nurse aged 45. Seventeen years ago livedo reticularis was first noticed over the left shin, and there was gradual extension until it now covers most of the legs, from which it extends below like a broad stirrup round the ankles on to the middle of the soles. Each summer the network has been the site of painful blisters, which discharge pale, yellow fluid, crust, and then heal, leaving small deep scars.

She has had for two years Raynaud attacks (10 to 15 minutes of numbness, pain, and skin colour changes—blue, white, red), affecting both the toes and the fingers. These may be provoked by heat (e.g. bath or bed) as well as cold, and occur in summer and winter.

The forearms also show slight livedo which appeared only a year ago. On the back of the left elbow there are a few of the same type of very small depressed linear or oval scars, which are present in greater numbers on the nodes of the vascular network on the legs. Several of these scars show a telangiectatic margin.

Blood-pressure 120/70. Blood-count normal, Wassermann, Kahn, and Mantoux tests negative. (No cold auto-agglutination of red blood cells.) Caloric test excited no capillary pulsation, suggesting the presence of organic disease of the digital vessels. The complete absence of palatal and corneal reflexes, and the patient's facies, might raise the question of artefact, but I believe this can be excluded.

This case recalls one described by Unna as asphyxia reticularis multiplex in the *International Atlas of Rare Skin Diseases* (Heft 10, 31), and this title seems more euphonious than, as well as taking precedence over, that of "inflammatory livedo reticularis".

Dr. Parkes Weber: I think that Unna's original term should be now discarded, as the case is obviously one of chronic symmetrical sclerodermia of the lower extremities with a kind of "cutis marmorata" in place of the more usual telangiectases or pigmentation. There is in this case also the association of sclerodermia with blanched toes. That, of course, is one of the most frequent associations of sclerodermia of the lower extremities; the analogous association in the upper limbs is perhaps still more frequent. The very marked involvement of the soles of the feet in the present case was pointed out to me by Dr. Freudenthal.

Dr. Robert Klaber: I suggested the use of this title, for lack of a better one. I find it quite impossible to accept Dr. Parkes Weber's view of the matter. These scars are present on the left elbow and elsewhere, without any of the thickening of the skin which is present on the lower third of the legs as a late secondary result. A section from a crusted lesion did suggest the possibility of a sclerodermatchange, but I do not think the clinical characters of the case are in any way altered by this.

Dr. Parkes Weber: I should be prepared to throw up my diagnosis if I heard that after five months and another biopsy chosen by Dr. Freudenthal, Dr. Klaber did not agree with me.

POSTSCRIPT (15/5/44) (R. K.).—Prosser Thomas (1942) showed a case in which there were recurrent bullæ on the right forearm as well as on the legs. In all three areas there was an underlying livedo reticularis, on which most of the bullæ occurred. Although labelled "Bullous Livedo from Heat" some doubt was expressed as to whether the bullæ were in fact excited by heat.

Wigley (1937) showed a "Case for Diagnosis" in which on the insteps and the middles of the soles were small symmetrical depressed scars surrounded by telangiectases. The woman had suffered from chilblains for many years and always had "a poor circulation". It seems probable that Prosser Thomas's case displayed only a less severe degree of the same condition, which Dr. Yorke has shown for me under the title of "Asphyxia Reticularis".

I strongly suspect that Wigley's case represents the end-result of a similar, though more localized process. The appearances of the scars, showing a stirrup-like distribution with surrounding telangiectases, was a part of the clinical picture in the case shown by Dr. Yorke.

One not rarely finds small solitary or grouped similar scars, especially round the ankle region, in some patients with marked varicose veins. Although there may have been past or present ulcers elsewhere, the patient emphatically denies ever having had any ulceration on the areas in question. The most that can be seen or elicited from the history is only a preceding scab or crust, comparable to those present in Dr. Yorke's case.

I believe that all these cases belong to a group of disorders which has so far lacked any comprehensive description or definition. A number of other cases have no doubt been shown in the past under a variety of titles, which provide no clue as to the nature of the underlying pathological process There can be little doubt that the skin changes described are secondary to peripheral vascular disease. This probably involves something more than hypostatic venous congestion. There is also in at least some of the cases, evidence of an abnormal capillary circulation and there may even be peripheral arterial disease, as in Dr. Yorke's case.

The peculiar skin scars might prove to be the result of an ischæmic necrosis involving only the deeper layers of the epithelium and hence not necessarily resulting in ulceration.

The title borrowed from Unna for this demonstration is admittedly archaic. For the moment, however, it has the outstanding advantage of pointing to the essential underlying vascular changes. Further investigation should eventually suggest a better term to cover this group of vasculo-dermal diseases.

REFERENCES
ADAMSON, H. G. (1916) *Brit. J. Derm.*, 28, 281.
THOMAS, E. W. PROSSER (1942) *Brit. J. Derm.*, 54, 183.
WIGLEY, J. E. M. (1937) *Brit. J. Derm.*, 49, 334.

Naevus Cutis Verticis Gyratus.—Robert Klaber, M.D.

Fishmonger aged 43. The condition on the scalp has not materially altered since its appearance at birth. He has been able for years to carry fish-boxes upon his head without any discomfort. The scalp shows from seven to ten well marked "convolutions" covering the greater part of the left side of the scalp, from which it extends a little over the midline (fig. 1). The occiput shows a large lobed fleshy naevus with several blue areas suggesting deep pigmentation (fig. 2). The frontotemporal margin of the main convoluted

FIG. 1. FIG. 2.

Nævus cutis verticis gyratus.

area shows a fairly deep pigmentation. These facts, together with the presence of large numbers of pigmented moles on the trunk and lower limbs, suggest that the "convolutions" also result from a naevus.

Dr. F. Parkes Weber: If Dr. Klaber had simply entitled this case "cutis verticis gyrata" there might have been some discussion, but as he has called it a "nævus gyratus" of the skin of the top of the head there can be no difference of opinion, because he has thereby truly described the whole condition together with its nature. The differential diagnosis from acromegalic and other forms of cutis verticis gyrata might have been discussed, but he has precluded that by calling the condition a "nævus gyratus," and everybody is agreed that this type of cutis gyrata is a nævus.

Erythema Annulare Centrifugum (Darier).—Robert Klaber, M.D.

Girl aged 18, in good general health. She has a three weeks' history only, of multiple centrifugal rings on cheeks and forehead, only very slightly raised and pink. There is slight irritation and increased redness in the evenings. No visible scaling, teeth and tonsils show no gross sepsis, and there are no signs of any epidermophytosis which Sutton and Sutton found in three of their cases. Sinuses not yet investigated.

The President: There were very faintly marked rings on the forehead and cheeks. I do not know what else it could be if not erythema annulare centrifugum. She said that the lesions did enlarge.

Asphyxia Reticularis Multiplex (Unna).—G. Allan Yorke, M.R.C.S., L.R.C.P. (for Dr. Robert Klaber).

Nurse aged 45. Seventeen years ago livedo reticularis was first noticed over the left shin, and there was gradual extension until it now covers most of the legs, from which it extends below like a broad stirrup round the ankles on to the middle of the soles. Each summer the network has been the site of painful blisters, which discharge pale, yellow fluid, crust, and then heal, leaving small deep scars.

She has had for two years Raynaud attacks (10 to 15 minutes of numbness, pain, and skin colour changes—blue, white, red), affecting both the toes and the fingers. These may be provoked by heat (e.g. bath or bed) as well as cold, and occur in summer and winter.

Fox-Fordyce Disease.—F. G. SHERRY-DOTTRIDGE, M.B.

Miss V. F. aged 16. Two years ago itchy pimples appeared in the axillæ and the condition has spread until the whole of both axillary areas are now covered with a rough nutmeg-grater-like follicular rash. Nipple and pubic areas are normal. Irritation is at times intense but does not appear to be connected with menstruation. Menstruation commenced at 13½ and is normal. Family history nil. The histology is typical of the condition.

The President: In this case there appeared to be papules in both axillæ, but not anywhere else. One patient of mine improved to a considerable extent with stilbœstrol. Then she became pregnant, and after a month or two of pregnancy the rash entirely —or very nearly entirely—disappeared. She is now coming on towards term, and it will be interesting to see what happens after confinement. There is some scarring where the papules were, but she has very little irritation now, and certainly no papules. Dr. Sherry-Dottridge tells me that stilbœstrol applied locally has no effect. I think stilbœstrol by mouth might be worth trying.

Urticaria Pigmentosa, Adult Type.—F. G. SHERRY-DOTTRIDGE, M.B.

Mrs. A. R. aged 38. Seventeen years ago on returning from a summer holiday she noticed bright red itchy spots on extensor surface of the forearms. This was regarded as sunburn. Some spots became small raised white wheals, whilst others remained flat. Later brownish marks were noticed. The condition has gradually appeared over the whole body, but latterly all lesions have remained flat. Irritation is intermittent.

Present condition.—Patient is rather obese but otherwise healthy. Scattered over the limbs and body generally are erythematous macular lesions of various sizes. Over the backs of the arms they have coalesced to form bright red plaques. Pigmented macular lesions are most marked on the forearm. The lesions nowhere appear urticarial. A few small deeply pigmented moles are present on the trunk.

Histology (Dr. Lowenberg).—Scattered through the corium are numerous mast cells— both spindle and oval shaped. Some can be found close to the junction of the epidermis and corium, singly or in small groups, but there is no tumour-like accumulation of mast cells. There is some hyper-pigmentation in the basal cell layer. Both intra- and inter-cellular œdema can be seen in the rete malpighi.

Dr. Parkes Weber: This is a case of what I described under the heading of telangiec-tasia macularis eruptiva perstans, that is to say, a form of urticaria pigmentosa char-acterized by a capillary telangiectatic condition rather than by pigmentation, in fact, as Dr. Freudenthal suggests, a "telangiectatic type" of urticaria pigmentosa.

The condition in the present case started many years ago in an "eruptive" way and has increased since then by occasional "eruptive bouts", or fresh crops of small telangiec-tatic maculæ.

Alopecia, Possibly Due to Ichthyosis.—C. H. WHITTLE, M.D.

B. G., a boy aged 13. Since aged 5 history of scurfiness and inflammation of scalp. He was first seen December 1942 when the scalp was very scurfy and septic. The toe-nails and thumb-nails also showed dirty discoloration, much thickening and roughening. The scalp responded well to treatment with tar and sulphathiazole locally but he remained under treatment for only a fortnight, and did not attend hospital again until 17.4.44.

He has now lost considerable amounts of scalp hair in patches 3 to 4 in. in diameter, on which the hairs are scanty, broken off short to ½ in. or so in length, coarse and wiry. There is much hyperkeratosis around the hair-follicles in the affected bare and scurfy areas. The scales are thick, adherent and dry.

The nails of thumbs, middle and index fingers show gross thickening, grey discolora-tion and accumulation of debris under their free margins. The big toe-nails show gryphotic thickening.

The eyebrows are partly lost, and most of the eyelashes are gone. The skin generally is dry and shows mild ichthyosis.

The scalp hair does not fluoresce under Wood light. Microscopic examination of hairs, scales and nail scrapings shows no sign of fungus elements.

Other features.—The child is small for his years and thin. He was born without any tear-ducts and an attempt by ophthalmologists to make good this defect has not been successful. He is active and athletic.

Family history.—Nothing relevant.

Diagnosis.—Keratosis pilaris, a form of ichthyosis: cause unknown. Vitamin A and C estimations in the blood plasma are being made.

Dr. L. Forman: I have shown a rather similar case (*Proc. Roy. Soc. Med.*, 1933, 27, 293), but without the general dryness of the skin, in a girl with similar history. She had

Chronic Buccal Moniliasis.—G. ALLAN YORKE, M.R.C.S., L.R.C.P. (for Dr. ROBERT KLABER).

Petty officer aged 25. During the first year of life (aged 4 months) he developed a condition of the tongue diagnosed by his doctor as "thrush". This persisted despite initial and subsequent treatment at several London hospitals, apart from a period of six months in 1938 after local application of pig. gentian violet 2/1,000 prescribed by Dr. Wigley. The condition fluctuates with his general health—deterioration being specially evident following exposure and malnutrition when shipwrecked. He was admitted to hospital primarily for treatment of a fungus infection of his toe clefts and groins.

Examination showed no dental caries or sepsis; on the upper lip there were two indented scars, and at the angles of the mouth radiating indurated fissures covered with a white plaque. The dorsum of the tongue is darker than normal; centrally the mucous membrane is divided into roughened, raised circular or oval areas. The fore-part is covered with a pale, smooth, shining adherent membrane passing with irregular outline towards the periphery, which is atrophic. There is a small palpable non-tender gland in the right cervical region.

The tongue and angles of the mouth are responding to treatment by local application of carbolfuchsin paint daily and potassium iodide gr. xxx t.d.s.

Dr. Duncan reported: *Monilia albicans* in films and culture from the tongue and lip, as well as from toes and groin. Dr. Duncan added that he personally had little doubt that this organism had been the primary cause of his tongue infection which appeared to date from a severe attack of thrush in infancy.

Dr. J. E. M. Wigley: This is the same patient I showed here in February 1929 (*Brit. J. Derm.*, 1929, 41, 274). At that time the condition of his tongue, which had been present for sixteen months, did not seem to cause him any appreciable pain or discomfort. It was large and pale, with a thickened, smooth surface, traversed by several fissures of moderate depth. On the surface were several greyish-yellow "washleather" patches which did not rub off. Deep rhagades were present at both angles of the mouth. The Wassermann reaction was negative and antisyphilitic treatment did not affect the clinical condition.

Subsequent to that publication his tongue was examined for the presence of Monilia with a positive result. It is of great interest to me to see how little his tongue has changed in fifteen years.

Dr. Robert Klaber: A similar case has been recently reported in which death occurred after a few months as a result of a monilial meningitis.

Dr. H. J. Wallace: I remember a woman aged 40, in whom monilia had been present for eight years. She had an infection of mouth, tongue, and nails which resisted all treatment and presented a picture very similar to this one, except that the angles of the mouth were spared. I found in the literature three or four references describing a like condition.

Dr. G. Duckworth: I had a similar case at St. John's affecting the buccal mucosa and the tongue, and the gluteal cleft. He cleared up, temporarily at least, on gentian violet, internally, gr. i, t.d.s. for five days at a time.

Lupus Erythematosus.—H. J. WALLACE, M.D. (for G. B. DOWLING, M.D.).

H. C., female aged 33. Case of lupus erythematosus of the classical fixed type, forming chiefly a band which extends across the nose from one malar region to the other. It began after a sun-burn nearly six years ago. She is presented because of an associated tuberculous adenopathy of wide distribution.

For some sixteen years she has had adenitis of both axillæ and neck. At times these glands have been voluminous but have never shown the least sign of breaking down. One of them was excised from the left axilla for biopsy; it showed tuberculous change of the ordinary type with caseation.

What is the nature of the relationship between the tuberculous glands and the skin changes? I can remember two other cases in which, during the course of lupus erythematosus tuberculous glands of the same hyperplastic non-caseating type appeared in the neck. In one, a gland which was excised on account of the possibility of lymphadenoma proved to be tuberculous. I do not, however, think that the association of lupus erythematosus and tuberculous adenopathy is particularly common.

The President: It was said that this particular gland was caseating.

Dr. Wallace: I have seen this case clinically for some years and there has been no sign of breaking down. The only caseation which was visible was microscopic.

Dr. F. G. Sherry-Dottridge: I have had one case of lupus erythematosus which had been treated by snow some years ago, and which showed a slight extension around the edge of the scar on the cheek. About two years ago the patient developed a painful swelling above the right clavicle. I sent her to a surgeon, who aspirated and found tubercle bacilli. It took a long time to heal.

It is not evident from the notes available what diagnosis was reached regarding this illness.

Early in June 1943 he noticed small lumps on his arms, two lumps on the right foot and one below the left knee (now vanished, leaving a depressed scar).

At the end of June many small lumps had appeared over calves and he reported sick as one or two of them were discharging; for most of the previous month there had been aching in the back of the legs after standing. He stated that a bandage was applied to the legs and he was given to understand that he was being treated for ruptured varicose veins.

Later in the year the lumps spread on his arms and hands and he had increasing dryness and stuffiness of his nose with difficulty in breathing and occasional bloody discharge from his nostrils.

He was seen by a dermatologist, and the diagnosis of *leprosy* was made and he was admitted into a military hospital on 28.1.44.

On February 18, 1944, E.N.T. Specialist reported (*a*):—

Nose: Septum broadened. Left side: 5 small nodules not much bigger than split peas in septum with surrounding mucosa reddened. Right side: A little dry blood and crusted pus on front 1 in. of septum, which is superficially ulcerated with thickened inferior and posterior edges.

Larynx: Normal, also pharynx and nasopharynx.

Bacteriological report: (1) Nasal swab—teeming with *B. leprae*. (2) Biopsy of nodule from leg—epithelium intact. There is a mass of cellular granulation tissue containing enormous numbers of *B. leprae*.

On February 5, 1944, a course of ol. chaulmoogræ was begun with 10 minims b.d. by mouth. Ten days later this emulsion was increased to four times daily, but was stopped after a few days on account of nausea.

Differential blood-count.—Polys. 74%, lymphos. 22%, monos. 2%, eosinophils. 2%.

Clinical appearances.—General appearance: He presents a cheerful disposition, is fully conscious of the nature of his complaint and is anxious to co-operate with his medical advisers.

The nose is not particularly club-like, but is slightly broadened; the countenance does not show a leonine aspect.

Eyebrows: Bilateral thinning of hair, outer half, nodule present.

Face: Nodule, left cheek—smaller one, right cheek.

Ears: Small nodule bilaterally in lobes.

Palate: Small nodule in roof of hard palate beneath denture.

Nasal vestibule: Bleeds when swabbed. See E.N.T. Specialist's reports (*a*) and (*b*).

Trunk: Conspicuously free, but one or two palpable nodules on back.

Limbs: These show many nodular infiltrations of various stages of reaction, both as regards their position and colour. Some are frankly raised above the surface whilst the main substance of others is palpable beneath the skin; many lie mid-way between.

Position: There is some attempt at a symmetrical distribution of the nodules. The heaviest crop is evident on the ulnar and radial borders of the arms, on the back more than on the front of the forearms and less over the biceps than over the back of the upper arms. The palms are more affected than the dorsa of the hands.

The buttocks present a fading macular eruption in addition to nodules, and are well covered as are the legs throughout their whole length; the heaviest crop lies on the back of the legs. Only a very few nodules are evident on the soles.

No thickening of nerves at palpable points: no history of paraesthesiæ, except slight numbness in one arm once, no sensory anæsthesia determined to pin-prick and cotton-wool either in lesions or on unaffected skin.

Colour: The nodules vary; most are a violaceous colour, some are yellowish white, due to their more deep-seated position, with a superimposed covering of skin. On palpation these nodules slip under the finger, but of course are attached to the skin. On pressure the colour fades leaving a translucent appearance. One on the right thumb has burst and is protected by a gauze covering.

Subsequent investigations in England:—

Urine: Clear, albumin negative, sugar negative. No deposit present. Sterile on culture.

E.N.T. Specialist's report (*b*): 2.3.44.

Nose: Nodular, mottled pink and red appearance of all visible nasal mucosa in both nasal fossæ; bleeds easily on being touched. Some crusting on right (concave) side of septum.

Pharynx appears normal. Nasopharynx not well seen. Nasal swab: *B. leprae* present in moderate numbers. Ophthalmologist's report: Nothing abnormal seen.

marked keratosis pilaris over the limbs and trunk and disappearance of hair on the face and eyebrows. The scalp was rather similar to Dr. Whittle's case. I have watched the case now for over 10 years. The keratosis pilaris over the trunk and limbs has disappeared, but the atrophy over the scalp is permanent. I rather thought of it as a nævoid form, a variant from ichthyosis.

POSTSCRIPT.—The blood plasma vitamin A was 77 I.U. per 100 c.c., the carotene 131 I.U. per 100 c.c., and the ascorbic acid 0·26 mg.%. Though the A and C are on the low side treatment by large doses (e.g. 50,000 units by mouth of A daily) for two months has had no effect on the condition.—C. H. W. (27.9.44).

Lichen Plano-Pilaris.—HUGH W. GORDON, M.C., M.B.

This patient first came under observation on 18.11.43 with thickening of his left second toe-nail and a small lesion on his right thumb. A scraping was made for tinea which was negative, and the nails treated with X-ray. The lesions cleared up. One month later he reported an eruption on the penis which was a definite lichen planus. This is still present though much better. One month ago he reported intense irritation of the scalp, which on examination showed lesions suggestive of lichen plano-pilaris. Recently he reports that the hairs are breaking off.

From examination of this patient to-day very little remains of the lesions of the nails, there being only a little disorganization present at the base of the right thumb nail.

The typical lichen planus lesions of the penis have now cleared up, whether as a result of injections of bismuth or not, it is impossible to say.

The lesions of the scalp are certainly not typical of lichen plano-pilaris, being more in the nature of follicular plugging.

Mycosis Fungoides.—HUGH W. GORDON, M.C., M.B.

Healthy man aged 56; he developed an eruption on his legs eighteen months ago in Uganda. This has spread till it covers practically his whole body and is intensely irritating. In consequence he has been invalided home with a diagnosis of seborrhœic dermatitis. This patient was referred to me by Sir Philip Manson-Bahr.

On examination.—There is an indurated exfoliative dermatitis of the legs which is fairly confluent, but in some areas there is a suggestion of annular lesions which are slightly indurated. On the body there is to be seen a figurate parakeratotic eruption. His inguinal glands are enlarged and indurated, but there is no enlargement of the spleen and the blood-count is normal.

A tentative diagnosis of mycosis fungoides was made.

A section taken from an indurated area of the leg was shown.

Dr. W. Freudenthal: A biopsy from an eczematoid area on the leg shows throughout the section in the upper part of the cutis a dense infiltrate consisting mainly of mesoblastic elements amongst which are cells with pyknotic nuclei. The epidermal changes are small and obviously secondary. The biopsy confirms the diagnosis mycosis fungoides.

Glomus Tumour (Forearm).—GEOFFREY DUCKWORTH, M.R.C.P.

The patient is a taxidriver, aged 65. For five years he had complained of an excruciatingly painful nodule on the radial border of the right forearm. It was about 1 in. below the mid-point from the elbow to the wrist, and was approximately ¼ in. in diameter. It was slightly raised and pinkish in colour. It was exceedingly painful when touched. There was no history of local injury. The lesion was excised.

The diagnosis with a query was glomus tumour, and the histo-pathological report (Dr. Muende) states:

"Typical section of a glomus tumour, showing the characteristic, closely packed, myo-epithelial cells, arising from the walls of small vessels, and an overgrowth of blood sinuses."

(The section was available under the microscope.)

Nodular Leprosy.—MAJOR LANCELOT WILLS, R.A.M.C.

L/Bdr. H., aged 29, married with one child, is a regular soldier who has seen service in Hong Kong, Gibraltar and North Africa.

History.—November 1941: Treated three weeks in E.M.S. Hospital. The patient's statement on this illness is "I felt dizzy, had a high temperature 104° and was very ill. My temperature lasted about six days. There were four red spots raised above the skin, soft to touch and felt as if they might burst on pressure. One spot was on each leg, one on buttock and one higher up on back. They all disappeared in three weeks. I think that it was thought, at one time, that I might have had typhus".

tuberculous on section, and as gold injection had proved so toxic it was decided to try the effect of a small dose of N.A.B. 0·3 g. was given intravenously on March 3 and forty-eight hours later she complained of severe headache, then acute pain in the chest accompanied by dyspnœa and pains in the arms. Next day there was a recurrence of the pain and swelling of the wrists and ankles, together with the appearance of fresh necrotic lesions on the forehead, neck and pads of the finger-tips. A similar type of lesion appeared on the tongue and later became a painful ulcer. There was an associated pyrexia, 99-100° F., and marked mental depression. After this reaction, which I regarded as a unique example of a non-specific allergy, no further injections were given and a month later the patient was transferred to the country, where she remained in a convalescent home on a salt-free diet and occasional ultra-violet light courses for about six months. She returned to the hospital this afternoon to report progress, and all her symptoms, including the intractable leg ulcer, are now in abeyance.

Dr. W. Freudenthal: Dr. Semon's biopsy of a skin lesion showed a large amount of sarcoid and tuberculoid tissue in which after careful search a very small number of acid-fast bacilli were found. In addition to that, acid-fast granules were present. In connexion with these I should like to add a word of warning. Acid-fast granules alone, when found in skin sections, should always be interpreted with caution, as normally sweat glands contain acid-fast granules. This fact is not sufficiently known, and even experienced bacteriologists have mistaken these granules for the granular form of tubercle or leprosy bacilli.

[*May* 18, 1944]

Necrobiosis Lipoidica (Without Diabetes).—H. C. SEMON, M.D.

The patient, a bachelor of 35, enjoys excellent health, and there is nothing significant in his history. A brother suffers from psoriasis, a fact which in view of the modern theories of its pathogenesis from a disturbed hepatic function, is worthy of note.

The lesions which are present over the tibiæ of both legs first appeared without sub-jective symptoms about three and a half years ago. They have slowly developed and now consist of smooth, waxy or translucent butter-tinted plaques. Over the left shin these have coalesced to form a spearhead-shaped lesion with the point directed down-wards. It involves quite a third of the total surface of the front of the leg. A few dilated venules add to the bizarre appearances of this very characteristic example of the condition.

About three years ago he presented himself at Guy's and was seen by Dr. Forman, who made the original diagnosis. I sent him to the Path. Dept., Royal Northern Hospital, where certain investigations showed that he was not in any sense diabetic. The blood cholesterol was normal. The blood uric acid was 8 mg. instead of the usual 1 to 3 or 4 mg. per 100 c.c. which is regarded as normal. Could this have a pathogenic bearing on the case?

The treatment so far is a mere placebo, although Dr. Klaber informs me that the patients may respond remarkably well to the ordinary treatment for diabetes. Up to 1933 all cases showing this disease had been regarded as diabetic. Dr. Forman's original sections are under the microscope, but were not stained for fat at the time. Dr. Freudenthal is going to show the Section some examples of fat staining.

This case is a striking example of so-called necrobiosis lipoidica diabetica, but it is, I think, the third example shown in this Section in which no diabetes was present—an interesting commentary on the original assumption that diabetes is an essential concomitant.

Dr. Freudenthal demonstrated on the screen typical sections of a case of necrobiosis lipoidica.

Dr. H. W. Allen: Is necrobiosis almost always associated with some central necrosis of the lesions? This case is absolutely dissimilar from one of the same disease shown at the Section in December 1933 by Dr. Klaber (*see* coloured plate, *Proc. Roy. Soc. Med.*, 1933, 27, 714).

Dr. Robert Klaber: My case was, in a sense, a classical one because it was associated with diabetes. On the other hand, there were certain unusual features which had not hitherto been described and which were absent, I believe, from most of the other cases since reported. There were doubly-refracting crystals (presumed cholesterol) in the centre of the lipoid nodule. Further, the lesions involuted rapidly as the diabetes came under control, whereas in most of the other cases reported with diabetes, its treatment has not influenced the skin lesions at all. The present case, of course, is one without diabetes and of these there are now a considerable number on record. No ulceration is present in this case, though I do not think that this is an essential feature. It seems possible that these non-diabetic cases, like the one first shown here by Dr. Goldsmith, may be less liable to ulceration. The present case certainly resembles Goldsmith's case more closely than mine.

Blood-count (4.3.44).—Total white cells 10,600 per c.mm.

Differential white count: Polys. 74%, lymphos. 18%, monos. 7%, eosinophils. 1%.

Blood sedimentation rate (3.3.44).—52 mm. at 1 hr. (Westergren).

Treatment.—As the blood sedimentation rate was rather high it was thought better to give Alepol 3% intramuscularly twice a week rather than to give any intravenous or intradermal preparation for fear of provoking a lepra reaction. Nineteen injections were given commencing with 0·2 c.c. and gradually increasing to 5 c.c..

Comment.—At no time did he show any fever and only experienced a slight sweat the night after an injection which was given at midday. There was no pain in the nodules during treatment. He has not developed any fresh lesions, neither has there been any obvious regression of the nodules. The hands are slightly cyanotic, but no patches of anæsthesia or diminution in pain sense have become evident. There was very slight nasal discharge one month ago, now none.

I should like to have the opinion of the Section as regards further treatment and possibly prognosis. If one can get the sedimentation rate down to about 10 mm. (first hour) I think the prognosis is favourable. The Kahn test was positive on two occasions. A Wassermann reaction was not performed but there is no history of syphilis.

My thanks are due to Brigadier R. M. B. MacKenna, A.M.S., Consultant Dermatologist to the Army, for permission to present this case to the Section.

Dr. Wills: He will eventually have to be boarded out of the Army. It is the first case of leprosy that has come under my care.

The President: Most of the cases we have seen here in recent months have been mixed, but this is purely nodular.

Dr. J. E. M. Wigley: Can Major Wills say how long this man was on service in the East before reporting sick, and what were the conditions as regards louse or other infestation, contact with the native population, &c., during his service? I ask these questions in the faint hope of throwing some light on the possible incubation period of leprosy.

Dr. Wills: He was in Hong Kong and Gibraltar, but he was in barracks the whole time. It was in 1934 that he was in Hong Kong. He left England in March 1941, and reported sick in June 1943.

The President: When he has been boarded out of the Army perhaps you can get him into St. Giles' Homes for British Lepers.

Favus.—H. J. WALLACE, M.D.

Child, aged 6 years; has had relapsing sepsis of the head for the past two years. He has lived in Woking all his life. Favus was suspected because of the cicatricial patch on the vertex. The diagnosis was confirmed by the typical fungus appearance in some of the affected hairs. Typical scutula have not been seen. The scalp had a distinct musty smell on one occasion. There are eight other members of the family, and none of these is affected. The glabrous skin and nails are not affected. There is no history of contact with mice. The sepsis readily subsides on treatment with sulphathiazole cream.

Dr. J. E. M. Wigley: Dr. Goldsmith showed two cases of favus here in October 1943 who had lived in Hemel Hempstead all their lives. Dr. Barber also showed one in March 1942 who had always lived in Slough.

Papulonecrotic Tuberculide.—H. C. SEMON, M.D.

The patient, a hospital nurse aged 22, was first seen in the O.P. Dept. R.N. Hospital in October 1942, and admitted with a deep ulcer on the right leg and numerous active verrucose and papulonecrotic lesions, together with old healed scars of similar origin on the back, thighs, legs, and buttocks. These had been present for about a year and appeared to have followed acute rheumatism, tonsillitis and pericarditis in December 1941. On admission to the wards we found she had a negative Mantoux and W.R. test. No fungus on culture of purulent discharge from the ulcer and no tubercle bacilli were demonstrated. The histology was regarded as "simple inflammatory" on the first occasion it was examined, but a month later scrapings from the base of the ulcer were reported as definitely tuberculous in structure. The Mantoux test was therefore repeated and now gave a strongly positive reaction clinically resembling the papulonecrotic lesions on the back. On December 24, 1942, sanocrysin 0·075 g. was administered intravenously and on the next day the patient complained of aching of the knees, and fingers. Objectively there was a more or less general polyarthritis with some rise of temperature (99–100° F.) for several days. On December 28 I noted subungual hæmorrhages and small purpuric nodules on the soles. By January 4 all these symptoms had subsided and there appeared to be some improvement of the tubercular lesions. A month later the tonsils were enucleated without any reaction. On February 22, 1943, I curetted the ulcer on the right leg, and packed it with B.I.P. gauze. The scrapings from the lesion were pronounced...

tuberculous on section, and as gold injection had proved so toxic it was decided to try the effect of a small dose of N.A.B. 0·3 g. was given intravenously on March 3 and forty-eight hours later she complained of severe headache, then acute pain in the chest accompanied by dyspnœa and pains in the arms. · Next day there was a recurrence of the pain and swelling of the wrists and ankles, together with the appearance of fresh necrotic lesions on the forehead, neck and pads of the finger-tips. A similar type of lesion appeared on the tongue and later became a painful ulcer. There was an associated pyrexia, 99-100° F., and marked mental depression. After this reaction, which I regarded as a unique example of a non-specific allergy, no further injections were given and a month later the patient was transferred to the country, where she remained in a convalescent home on a salt-free diet and occasional ultra-violet light courses for about six months. She returned to the hospital this afternoon to report progress, and all her symptoms, including the intractable leg ulcer, are now in abeyance.

Dr. W. Freudenthal: Dr. Semon's biopsy of a skin lesion showed a large amount of sarcoid and tuberculoid tissue in which after careful search a very small number of acid-fast bacilli were found. In addition to that, acid-fast granules were present. In connexion with these I should like to add a word of warning. Acid-fast granules alone, when found in skin sections, should always be interpreted with caution, as normally sweat glands contain acid-fast granules. This fact is not sufficiently known, and even experienced bacteriologists have mistaken these granules for the granular form of tubercle or leprosy bacilli.

[May 18, 1944]

Necrobiosis Lipoidica (Without Diabetes).—H. C. SEMON, M.D.

The patient, a bachelor of 35, enjoys excellent health, and there is nothing significant in his history. A brother suffers from psoriasis, a fact which in view of the modern theories of its pathogenesis from a disturbed hepatic function, is worthy of note.

The lesions which are present over the tibiæ of both legs first appeared without subjective symptoms about three and a half years ago. They have slowly developed and now consist of smooth, waxy or translucent butter-tinted plaques. Over the left shin these have coalesced to form a spearhead-shaped lesion with the point directed downwards. It involves quite a third of the total surface of the front of the leg. A few dilated venules add to the bizarre appearances of this very characteristic example of the condition.

About three years ago he presented himself at Guy's and was seen by Dr. Forman, who made the original diagnosis. I sent him to the Path. Dept., Royal Northern Hospital, where certain investigations showed that he was not in any sense diabetic. The blood cholesterol was normal. The blood uric acid was 8 mg. instead of the usual 1 to 3 or 4 mg. per 100 c.c. which is regarded as normal. Could this have a pathogenic bearing on the case?

The treatment so far is a mere placebo, although Dr. Klaber informs me that the patients may respond remarkably well to the ordinary treatment for diabetes. Up to 1933 all cases showing this disease had been regarded as diabetic. Dr. Forman's original sections are under the microscope, but were not stained for fat at the time. Dr. Freudenthal is going to show the Section some examples of fat staining.

This case is a striking example of so-called necrobiosis lipoidica diabetica, but it is, I think, the third example shown in this Section in which no diabetes was present—an interesting commentary on the original assumption that diabetes is an essential concomitant.

Dr. Freudenthal demonstrated on the screen typical sections of a case of necrobiosis lipoidica.

Dr. H. W. Allen: Is necrobiosis almost always associated with some central necrosis of the lesions? This case is absolutely dissimilar from one of the same disease shown at the Section in December 1933 by Dr. Klaber (see coloured plate, *Proc. Roy. Soc. Med.*, 1933, **27**, 714).

Dr. Robert Klaber: My case was, in a sense, a classical one because it was associated with diabetes. On the other hand, there were certain unusual features which had not hitherto been described and which were absent, I believe, from most of the other cases since reported. There were doubly-refracting crystals (presumed cholesterol) in the centre of the lipoid nodule. Further, the lesions involuted rapidly as the diabetes came under control, whereas in most of the other cases reported with diabetes, its treatment has not influenced the skin lesions at all. The present case, of course, is one without diabetes and of these there are now a considerable number on record. No ulceration is present in this case, though I do not think that this is an essential feature. It seems possible that these non-diabetic cases, like the one first shown here by Dr. Goldsmith, may be less liable to ulceration. The present case certainly resembles Goldsmith's case more closely than mine.

Blood-count (4.3.44).—Total white cells 10,600 per c.mm.

Differential white count: Polys. 74%, lymphos. 18%, monos. 7%, eosinophils. 1%.

Blood sedimentation rate (3.3.44).—52 mm. at 1 hr. (Westergren).

Treatment.—As the blood sedimentation rate was rather high it was thought better to give Alepol 3% intramuscularly twice a week rather than to give any intravenous or intradermal preparation for fear of provoking a lepra reaction. Nineteen injections were given commencing with 0·2 c.c. and gradually increasing to 5 c.c.

Comment.—At no time did he show any fever and only experienced a slight sweat the night after an injection which was given at midday. There was no pain in the nodules during treatment. He has not developed any fresh lesions, neither has there been any obvious regression of the nodules. The hands are slightly cyanotic, but no patches of anæsthesia or diminution in pain sense have become evident. There was very slight nasal discharge one month ago, now none.

I should like to have the opinion of the Section as regards further treatment and possibly prognosis. If one can get the sedimentation rate down to about 10 mm. (first hour) I think the prognosis is favourable. The Kahn test was positive on two occasions. A Wassermann reaction was not performed but there is no history of syphilis.

My thanks are due to Brigadier R. M. B. MacKenna, A.M.S., Consultant Dermatologist to the Army, for permission to present this case to the Section.

Dr. Wills: He will eventually have to be boarded out of the Army. It is the first case of leprosy that has come under my care.

The President: Most of the cases we have seen here in recent months have been mixed, but this is purely nodular.

Dr. J. E. M. Wigley: Can Major Wills say how long this man was on service in the East before reporting sick, and what were the conditions as regards louse or other infestation, contact with the native population, &c., during his service? I ask these questions in the faint hope of throwing some light on the possible incubation period of leprosy.

Dr. Wills: He was in Hong Kong and Gibraltar, but he was in barracks the whole time. It was in 1934 that he was in Hong Kong. He left England in March 1941, and reported sick in June 1943.

The President: When he has been boarded out of the Army perhaps you can get him into St. Giles' Homes for British Lepers.

Favus.—H. J. WALLACE, M.D.

Child, aged 6 years; has had relapsing sepsis of the head for the past two years. He has lived in Woking all his life. Favus was suspected because of the cicatricial patch on the vertex. The diagnosis was confirmed by the typical fungus appearance in some of the affected hairs. Typical scutula have not been seen. The scalp had a distinct musty smell on one occasion. There are eight other members of the family, and none of these is affected. The glabrous skin and nails are not affected. There is no history of contact with mice. The sepsis readily subsides on treatment with sulphathiazole cream.

Dr. J. E. M. Wigley: Dr. Goldsmith showed two cases of favus here in October 1943 who had lived in Hemel Hempstead all their lives. Dr. Barber also showed one in March 1942 who had always lived in Slough.

Papulonecrotic Tuberculide.—H. C. SEMON, M.D.

The patient, a hospital nurse aged 22, was first seen in the O.P. Dept. R.N. Hospital in October 1942, and admitted with a deep ulcer on the right leg and numerous active verrucose and papulonecrotic lesions, together with old healed scars of similar origin on the back, thighs, legs, and buttocks. These had been present for about a year and appeared to have followed acute rheumatism, tonsillitis and pericarditis in December 1941. On admission to the wards we found she had a negative Mantoux and W.R. test. No fungus on culture of purulent discharge from the ulcer and no tubercle bacilli were demonstrated. The histology was regarded as "simple inflammatory" on the first occasion it was examined, but a month later scrapings from the base of the ulcer were reported as definitely tuberculous in structure. The Mantoux test was therefore repeated and now gave a strongly positive reaction clinically resembling the papulonecrotic lesions on the back. On December 24, 1942, sanocrysin 0·075 g. was administered intravenously and on the next day the patient complained of aching of the knees, and fingers. Objectively there was a more or less general polyarthritis with some rise of temperature (99-100° F.) for several days. On December 28 I noted subungual hæmorrhages and small purpuric nodules on the soles. By January 4 all these symptoms had subsided and there appeared to be some improvement of the tubercular lesions. A month later the tonsils were enucleated without any reaction. On February 22, 1943, I curetted the ulcer on the right leg, and packed it with B.I.P. gauze. The scrapings from the lesion were pronounced as

Lieut.-Colonel F. F. Hellier: In one case I saw in which gold injections were given, the skin after exposure to light acted rather like a photographic plate. The patient developed a purple colour. Fortunately in this patient it was not persistent and cleared up. Possibly a somewhat similar action may occur in argyria.

Dr. Robert Klaber: I have seen cases of "traumatic argyria" in a small factory which uses silver fulminate in preference to fulminate of mercury for the strip inside the Christmas crackers which produces the "bang". However these cases have been less numerous than those affected by dermatitis.

Lupus Erythematosus.—E. H. Molesworth, M.D., F.R.A.C.P. (*in absentia*).

Mrs. R. R., a middle-aged woman, living at Leura, New South Wales (elevation nearly 3,000 ft.). Present condition has been developing for three years. Now practically the whole of the face and neck (except at back) are involved. The hands and forearms are not affected. The active edges everywhere are red, prominent and almost verrucose. The follicles are prominent in the active areas, but absent altogether in the scarred patches, which are dead white. The condition extends down the front and sides of the neck, but the back of the neck, where the skin is protected by the hair, is quite clear. The V area in the region of the manubrium sterni is involved. There does not seem to be any doubt that the condition is one of lupus erythematosus, but it is unusual in type. The patient's home was in the mountains, where the sun is very bright even in winter, and, in addition, the winter is very cold with frosts daily and snow frequently. Distribution suggests provocative action by sunlight. The hands are not affected because the patient was accustomed to wear gloves almost always when out in the open. No focus of infection or evidence of tuberculosis could be discovered, although Dr. A. Macintosh made a very extensive search for any such condition, and, apart from the lupus erythematosus, the patient seemed to be very healthy. (The Honorary Secretary read the case reports. Coloured photographs and a histological section were shown.)

Dr. G. B. Dowling: I recall the case of an elderly woman who had bright red areas of subacute lupus erythematosus on the feet and hands as well as on the face and neck. Pituitrin was tried for its blanching effect, a daily dose of 1 c.c. The effect appeared to be remarkable, the condition settling down in about three weeks. I have found pituitrin occasionally useful in other erythematous conditions, such as the acute exudative phase of psoriasis, and in an acute violently red seborrhœic eczema of the scalp and face.

The President: Does the blanching occur at once?

Dr. Dowling: Yes, very soon.

The President: Perhaps this will provide an explanation of the relief of pain in herpes zoster with pituitrin.

Dr. Freudenthal: The section confirms Dr. Molesworth's diagnosis of lupus erythematosus.

Dr. Robert Klaber: I have certainly seen pituitrin prove effective in rosacea. With regard to other treatment for lupus erythematosus, the use of mapharside has been recommended in America. I have only used it recently in one long-standing case, in which there was no response to bismuth or gold injections. After a few injections, each of 0.04 g., there has been some definite improvement.

Dr. Louis Forman: Superficial erythematous lupus erythematosus is the type usually selected for treatment with sulphonamide. I believe these patients readily become sensitive to sulphonamides, and the associated sulphonamide erythema is frequently more severe around the lupus erythematosus areas, or a flare-up around the lupus erythematosus areas may be the only cutaneous reaction. When this subsides, the lupus erythematosus may have improved. This sequence may be no more than a response to a non-specific reaction.

One must be prepared for frequent cutaneous reactions associated with fever. One case which particularly impressed me was that of a young woman with a relapse of superficial lupus erythematosus. Some months previously she had been given sulphonamide with some improvement, but she said that she felt ill while taking the drug. I took the precaution of giving half a tablet, i.e. ¼ g. only but within half an hour, she complained that she felt ill, her skin became pale, her pulse was imperceptible, and she remained in this severely collapsed condition over night, in spite of resuscitation procedures.

Dr. A. N. P. Milner: A case of lupus erythematosus came to me which had failed to respond to gold, bismuth and other treatments. I gave her an intracutaneous injection of moogrol into one lesion in the lateral frontal area close to the left orbit. Only 0.3 c.c. was given. Unfortunately a small amount leaked into the subcutaneous tissue. There was a severe reaction with erythema and considerable œdema which extended to both eye-lids. This settled down with sedative treatment and the lesion healed completely without scarring. Subsequently other lesions were treated more accurately with intracutaneous injections of moogrol, with slight reaction but no healing. I do not consider one is justified in view of this reaction, to give moogrol subcutaneously into the lesions.

Dr. W. N. Goldsmith: The majority of cases published in recent years have been non-ulcerating. Referring to the original case of mine to which Dr. Klaber has alluded, I saw this case six years later and have been intending to publish it. She developed a number of nodules on the thigh which corresponded to Oppenheim's description of the primary lesion. The patient had a very striking family history of tuberculosis, and she herself had had erythema nodosum in the affected leg. While under observation on the second occasion, she was subjected to a Mantoux test which caused a focal reaction around all the lesions, so that at that time I felt rather strongly suspicious that tuberculosis must have something to do with the skin condition. Altogether one wonders whether the primary change is the nécrobiosis or the cellular infiltrate. In granuloma annulare, where there is also a peculiar necrosis, one feels nevertheless that the condition is primarily a granuloma and not primarily a necrosis. In another case of mine there was no tuberculosis, but there was severe vascular disease and diabetes; she had, among others, a lesion on the forearm, which is rare. Dr. Freudenthal excised a very recent and small nodule, only about 0·5 cm. broad, and this showed areas of cellular infiltrate, and hardly a trace of necrosis.

The President: You mean areas of cellular infiltration?

Dr. Goldsmith: Yes, cellular infiltration. The point is whether the cellular infiltration is a reaction to the necrobiosis or is itself the first change.

The President: What about the high blood uric acid? Did you come across any other case with that peculiarity?

Dr. Semon: No, this is my first case of necrobiosis, I have looked up the literature and have not found any reference to blood uric acid estimations in this connexion.

Dr. Louis Forman: This patient had his fasting blood uric acid and cholesterol estimated in 1941 at Guy's. In 1941 the uric acid was 4·2 milligrams per 100 c.c., i.e. at the top limit of normal, and the serum cholesterol was 168 milligrams per 100 c.c. Unfortunately the material could not be stained for fat because we could not fix the section in alcohol, and I think the biopsy took rather a long time to heal.

Occupational Argyria.—J. E. M. WIGLEY, M.B., and P. M. DEVILLE, M.D.

Man aged 61. He has been in the silver trade most of his life, apparently in that part concerned with the manufacture of silver nitrate crystals. He began to develop the pigmentation about ten years ago. He is a healthy-looking man. There is a grey to black pigmentation extending over his forehead, the upper part of his face, on the backs of his hands, and forearms. The caruncles at the inner canthi of his eyes are quite black, and the conjunctivæ apparently stippled with black. On the upper V portion of his chest are discrete greyish-black macular areas which are also present on the back. The patient told me that his hair occasionally goes bright yellow and seems to fall out, and at times his underwear is blackened. He very closely resembles the coloured illustration published by Harker and Hunter (Harker, J. M., and Hunter, D., *Brit. J. Derm.*, 1935, 47, 441), and I think he may be regarded as a very typical example of occupational argyria. It is hoped to investigate this case more fully.

The President: Is argyria subject to compensation on cosmetic grounds?

Dr. H. C. Semon: In my experience hitherto the point has not arisen, and I hope it will not. It certainly does not conform with the legal definition of dermatitis, and it does not interfere with the man carrying on his work. Argyria (medicamentosa) used to be fairly common at one time when silver nitrate was used for bladder washouts. In America some years ago there was a good deal of trouble on this score from proprietary preparations used for nasal catarrh.

P.S.:—Stillians, W. W., and Lawless, T. K. (*J. Amer. med. Ass.*, 1929, 92, 20), have claimed successful bleaching of the pigment by local injections of a mixture of 1% pot. ferrocyanide with 6% sodium thiosulphate.

The President: This man is not so black as the illustration of Hunter's case.

Dr. Louis Forman: I am interested in the appearance of skin in argyria under dark-ground illumination. In the case I showed at the British Association of Dermatology and Syphilis Meeting in June 1940, the patient had had a congenital fissured tongue with benign transitory plaques, and had used silver nitrate paint for five years. Her skin had become heavily pigmented. Sections demonstrated melanin in the epidermal cells and in cutis, but dark-ground illumination of slides stained by routine methods did not show refractile granules.

Hill and Montgomery (*Arch. Derm. Syph.*, Chicago, 1941, 44, 588-599) repeating Habermann's work, give good illustrations of cases of argyria examined under dark-ground illumination. It is best to carry out this examination using sections lightly stained with methylene blue. "With dark-ground illumination under low power, silver shows as yellowish white lines. Higher magnification reveals brilliantly refractile white granules".

The President: There is a paper by Firth, D., and Harrison, G. A. (*Brit. J. Derm.*, 1924, 36, 105), in which they figured sections showing the location of the silver in the epidermis.

Dr. W. Griffith: Silver nitrate pills were once a common remedy for epilepsy and often gave rise to this condition.

Lieut.-Colonel F. F. Hellier: In one case I saw in which gold injections were given, the skin after exposure to light acted rather like a photographic plate. The patient developed a purple colour. Fortunately in this patient it was not persistent and cleared up. Possibly a somewhat similar action may occur in argyria.

Dr. Robert Klaber: I have seen cases of "traumatic argyria" in a small factory which uses silver fulminate in preference to fulminate of mercury for the strip inside the Christmas crackers which produces the "bang". However these cases have been less numerous than those affected by dermatitis.

Lupus Erythematosus.—E. H. MOLESWORTH, M.D., F.R.A.C.P. (*in absentia*).

Mrs. R. R., a middle-aged woman, living at Leura, New South Wales (elevation nearly 3,000 ft.). Present condition has been developing for three years. Now practically the whole of the face and neck (except at back) are involved. The hands and forearms are not affected. The active edges everywhere are red, prominent and almost verrucose. The follicles are prominent in the active areas, but absent altogether in the scarred patches, which are dead white. The condition extends down the front and sides of the neck, but the back of the neck, where the skin is protected by the hair, is quite clear. The V area in the region of the manubrium sterni is involved. There does not seem to be any doubt that the condition is one of lupus erythematosus, but it is unusual in type. The patient's home was in the mountains, where the sun is very bright even in winter, and, in addition, the winter is very cold with frosts daily and snow frequently. Distribution suggests provocative action by sunlight. The hands are not affected because the patient was accustomed to wear gloves almost always when out in the open. No focus of infection or evidence of tuberculosis could be discovered, although Dr. A. Macintosh made a very extensive search for any such condition, and, apart from the lupus erythematosus, the patient seemed to be very healthy. (The Honorary Secretary read the case reports. Coloured photographs and a histological section were shown.)

Dr. G. B. Dowling: I recall the case of an elderly woman who had bright red areas of subacute lupus erythematosus on the feet and hands as well as on the face and neck. Pituitrin was tried for its blanching effect, a daily dose of 1 c.c. The effect appeared to be remarkable, the condition settling down in about three weeks. I have found pituitrin occasionally useful in other erythematous conditions, such as the acute exudative phase of psoriasis, and in an acute violently red seborrhœic eczema of the scalp and face.

The President: Does the blanching occur at once?

Dr. Dowling: Yes, very soon.

The President: Perhaps this will provide an explanation of the relief of pain in herpes zoster with pituitrin.

Dr. Freudenthal: The section confirms Dr. Molesworth's diagnosis of lupus erythematosus.

Dr. Robert Klaber: I have certainly seen pituitrin prove effective in rosacea. With regard to other treatment for lupus erythematosus, the use of mapharside has been recommended in America. I have only used it recently in one long-standing case, in which there was no response to bismuth or gold injections. After a few injections, each of 0·04 g., there has been some definite improvement.

Dr. Louis Forman: Superficial erythematous lupus erythematosus is the type usually selected for treatment with sulphonamide. I believe these patients readily become sensitive to sulphonamides, and the associated sulphonamide erythema is frequently more severe around the lupus erythematosus areas, or a flare-up around the lupus erythematosus areas may be the only cutaneous reaction. When this subsides, the lupus erythematosus may have improved. This sequence may be no more than a response to a non-specific reaction.

One must be prepared for frequent cutaneous reactions associated with fever. One case which particularly impressed me was that of a young woman with a relapse of superficial lupus erythematosus. Some months previously she had been given sulphonamide with some improvement, but she said that she felt ill while taking the drug. I took the precaution of giving half a tablet, i.e. ½ g. only but within half an hour, she complained that she felt ill, her skin became pale, her pulse was imperceptible, and she remained in this severely collapsed condition over night, in spite of resuscitation procedures.

Dr. A. N. P. Milner: A case of lupus erythematosus came to me which had failed to respond to gold, bismuth and other treatments. I gave her an intracutaneous injection of moogrol into one lesion in the lateral frontal area close to the left orbit. Only 0·3 c.c. was given. Unfortunately a small amount leaked into the subcutaneous tissue. There was a severe reaction with erythema and considerable œdema which extended to both eye-lids. This settled down with sedative treatment and the lesion healed completely without scarring. Subsequently other lesions were treated more accurately with intra-cutaneous injections of moogrol, with slight reaction but no healing. I do not consider one is justified in view of this reaction, to give moogrol subcutaneously into the lesions.

Dr. A. M. H. Gray: Some years ago I tried the effect of sodium morrhuate in lupus erythematosus, with no results whatever. Years ago, when salvarsan first came in, it was looked upon as the best remedy for lupus erythematosus in the days before bismuth or gold was thought of. Then silver salvarsan was very popular for a time, but it was distinctly uncertain in its action. I should say that of the metallic salts gold is the best so far in its action. I shall be interested to hear of any experience with sulphonamide drugs. I am profoundly sceptical about the streptococcal origin of chronic lupus erythematosus, and I should not expect the compound to have any effect except possibly in some very acute cases.

Dr. W. N. Goldsmith: I should like to support entirely what Dr. Gray has said concerning the arsphenamines. I had an exceedingly severe case lately which was unusually ulcerated. The Wassermann reaction was negative. The patient had been treated with gold and bismuth without improvement, and he healed very rapidly with ordinary arsphenamine. As regards the sulphonamides, my experience is small, but it has always made my cases worse.

Dr. Robert Klaber: I agree with the disappointment generally expressed concerning sulphonamide treatment of chronic cases, but I have had an acute disseminate case which responded dramatically two years ago. The erythrocyte sedimentation rate in this patient, which was nearly 100, has taken these two years to come gradually down to its present rate of about 30. The patient still has slight joint pains but the skin lesions are not active.

The President: Was the patient treated with short courses?

Dr. Klaber: She was treated, in the first instance, intensively, followed by a period of small doses.

The President: My experience of the sulphonamides is very much the same as that of others who have spoken. A recent case in which there was extensive lupus erythematosus on the face did seem to improve with sulphonamides, but that is almost the only case I can remember that did so. Nearly all the others either did not improve or else became ill and had to give up the treatment. The curious thing about the treatment of lupus erythematosus is that different kinds of gold salts appear in some cases to make a great difference. One patient, a doctor, had severe lupus erythematosus and various sorts of gold had been tried. I suggested that a trial should be made with lopion, and this was astonishingly successful so that her lupus erythematosus very nearly disappeared altogether. I do not know whether it is the usual experience that one sort of gold is more effective than another. I think that gold given intramuscularly is more likely to cause dermatitis than when given intravenously.

Section of Comparative Medicine

President—J. T. EDWARDS, M.R.C.V.S.

[*April* 19, 1944]

DISCUSSION ON THE LIMITATIONS AND USES OF THE COMPARATIVE METHOD IN MEDICINE

IV. Neurology and Psychiatry

Dr. Ernest Jones (*Psycho-analysis and Comparative Physiology*): Psycho-analysis is the department of psychology which offers the best prospect of effecting a liaison with biology, including physiology, since the main direction of its work lies in the unravelling of complex mental processes and in the tracing of their genesis to a small number of primitive impulses which man shares with other animals. The deep prejudice man has against recognizing his kinship with the animal world was only partly overcome by the acceptance of the theory of evolution. Actually a compromise was reached, it being grudgingly agreed that man's body may have been derived from non-human origins provided that the same need not hold good for his mind. Here a claim was still asserted for a true uniqueness, and for an independent creation. The findings of psycho-analysis, if taken seriously, are making it increasingly difficult to sustain this belief, and are carrying the theory of evolution through to its logical conclusion by treating both mind and body from a genetic point of view.

We apply the Latin neutral and impersonal term "id" to that earliest and deepest layer of the mind that precedes any sense of individual self. The ego or self then slowly develops by the fusion of "ego nuclei" which are in connexion with various parts of the body, first the mouth and anus, later the hands, eyes, genital organs, and so on.

In spite of this we are unfortunately still far from the desirable state of being able to define the primitive mental elements that would enable us to make a start on the obscure problems of mental heredity in the way open in the fields where physical genes can be isolated. The old term "instinct", however much it may be criticized, stands for something real which is still in need of definition. Freud postulated two broad groups of immanent tendencies, one regressing towards simple states and ultimately towards the inorganic, i.e. death, and the other those striving to postpone this goal and even to renew life at its starting point. Although a similar idea had been put forth previously by biologists as well as by philosophers, we have not yet received an adequate criticism of it from those sides. An allied conception of his is that instincts are essentially conservative in nature in that their aim is to reinstate as far as possible some earlier state of affairs which has had to be abandoned through external pressure or other change in the environment. The periodic breeding migrations of salmon or eels furnish perhaps the most obvious example of this, but Freud thinks that the same principle underlies all instinctual action. It was indeed this conclusion that led him to postulate the tendency to reversion to the earliest state of all, namely lifelessness.

Freud was probably stimulated in this train of thought by his familiarity with a similar, though not identical, tendency that pervades all mental life and plays a very prominent part in psychopathological conditions: namely, the tendency to "regress", to revert to earlier stages in ontogenetic, and possibly also phylogenetic, development. It is likely that future study of the exact nature of this mental tendency will enable it to be linked up with similar ones in the physiological field and perhaps throw more light on the phenomena of atavism.

Apart from theoretical considerations, however, psycho-analysis can present many concrete studies in the field of instinct that should be of significance to the comparative

Dr. A. M. H. Gray: Some years ago I tried the effect of sodium morrhuate in lupus erythematosus, with no results whatever. Years ago, when salvarsan first came in, it was looked upon as the best remedy for lupus erythematosus in the days before bismuth or gold was thought of. Then silver salvarsan was very popular for a time, but it was distinctly uncertain in its action. I should say that of the metallic salts gold is the best so far in its action. I shall be interested to hear of any experience with sulphonamide drugs. I am profoundly sceptical about the streptococcal origin of chronic lupus erythematosus, and I should not expect the compound to have any effect except possibly in some very acute cases.

Dr. W. N. Goldsmith: I should like to support entirely what Dr. Gray has said concerning the arsphenamines. I had an exceedingly severe case lately which was unusually ulcerated. The Wassermann reaction was negative. The patient had been treated with gold and bismuth without improvement, and he healed very rapidly with ordinary arsphenamine. As regards the sulphonamides, my experience is small, but it has always made my cases worse.

Dr. Robert Klaber: I agree with the disappointment generally expressed concerning sulphonamide treatment of chronic cases, but I have had an acute disseminate case which responded dramatically two years ago. The erythrocyte sedimentation rate in this patient, which was nearly 100, has taken these two years to come gradually down to its present rate of about 30. The patient still has slight joint pains but the skin lesions are not active.

The President: Was the patient treated with short courses?

Dr. Klaber: She was treated, in the first instance, intensively, followed by a period of small doses.

The President: My experience of the sulphonamides is very much the same as that of others who have spoken. A recent case in which there was extensive lupus erythematosus on the face did seem to improve with sulphonamides, but that is almost the only case I can remember that did so. Nearly all the others either did not improve or else became ill and had to give up the treatment. The curious thing about the treatment of lupus erythematosus is that different kinds of gold salts appear in some cases to make a great difference. One patient, a doctor, had severe lupus erythematosus and various sorts of gold had been tried. I suggested that a trial should be made with lopion, and this was astonishingly successful so that her lupus erythematosus very nearly disappeared altogether. I do not know whether it is the usual experience that one sort of gold is more effective than another. I think that gold given intramuscularly is more likely to cause dermatitis than when given intravenously.

spinal roots and tracts within the cord. Of particular interest is the condition known as Wernicke's encephalopathy, which is now known to be due to a deficiency of this vitamin.

(7) *Tumours.*—Spontaneous neoplasms of the C.N.S. in animals may be commoner than is supposed. Recently, in the U.S.A., the experimental introduction into the brains of mice of pellets containing methyl cholanthrene. and more recently benzpyrene, has induced the growth of various meningeal and glial tumours.

(8) *Therapeutic trials.*—No account of animal experimentation would be complete without mentioning the trial of new therapeutic agents, including various antibacterial substances. Experiments on the brain with compounds such as the acridine antiseptics, sulphonamide and penicillin have been helpful in the treatment of wounds involving the brain and meninges. It should be obligatory that any therapeutic agent, whether chemical or physical, should be submitted to such tests before being tried on the human body.

REFERENCES

GRÜNEBERG, H. (1944) *Proc. Roy. Soc. Med.*, 37, 125.
HOWE, H. A., and BODIAN, D. (1942) Neural Mechanisms in Poliomyelitis. , London.
HUNTER, D., BOMFORD, R. R., and RUSSELL, D. S. (1940) *Quart. J. Med.*, 9, 193.
HURST, E. W. (1942) *Austral. J. Exp. Biol. and Med. Sci.*, 20, 297.
—— COOK, B. T., and MELVIN, P. (1943) *Austral. J. Exp. Biol. and Med. Sci.*, 21, 115.
INNES, J. R., RUSSELL, D. S., and WILSDON, A. J. (1940) *J. Path. Bact.*, 50, 455.
MELLANBY, E. (1941) *J. Physiol.*, 99, 467.

Dr. J. R. M. Innes (*Veterinary Research Laboratories, Wilmslow*): The purpose of the comparative study of diseases is not solely to shed light on human problems because animal studies have their intrinsic biological and utilitarian worth. A study of human diseases can be used for elucidation of animal problems for the simple reason that the fundamental principles of pathology were evolved originally by studies of human diseases and have since served as a basis for all veterinary work.

There is no real borderline between animal and human pathology and such differences which do exist are more apparent than real.

The medical worker begins with the advantage that there is more known about the human nervous system from all angles—anatomy, embryology, physiology and pathology —than the animal. An orderly system of classification of human nervous diseases has been built up, the scope of which increases as more knowledge is gained of the central nervous system as a functional organ. In the case of chronic progressive and relapsing conditions years may pass between disease inception and death. In such chronic diseases (of which there are many where experimental transmission is not yet possible) the human neurologist may have to be content with studying the end stages of a burnt-out process. The initial lesion must then be deduced or guessed at, and in the search for ætiological explanation any causal agent may have disappeared from the scene of damage. There are a number of human nervous diseases in which such a stage has been reached and it is here that animal studies might be most profitably used.

On the animal side there is a contrast between the amount of investigation which has been done on the comparative anatomy, physiology and histology (using the monkey, cat, dog and rat as type animals) and that on the comparative pathology of the central nervous system. Veterinary research workers have taken to a study of diseases of the animal nervous system often by accident with perhaps one or two outstanding exceptions, the most notable of which is work on animal virus encephalitides, which has contributed greatly to an understanding of encephalitis and the neurotropic viruses in man.

Accurate clinical diagnosis of animal nervous diseases is difficult simply because the symptoms can only be objective in character. We do not yet possess data, which could only accrue by detailed examinations of the nervous system of large numbers of different animals nor do we know as yet to what extent the obscurer nervous disorders of man occur in animals. Sporadic nervous disorders have not been studied very much and there must be many non-fatal diseases of animals with nervous manifestations during life which are missed and which must remain unexplained on a pathological basis. Systematic investigations of the state of the central nervous system in general animal disease have not been made. Modern neuropathological technique is only beginning to be used in the veterinary field.

Much is known on the structure and course of the fibre tracts in certain animal species, e.g. dog, cat, monkey and rat, although little in the cow, sheep and horse and only fragmentary data concerning the finer nature of pathological processes of animals as a whole. There have been no comparable systematic studies of the distribution of glial cells in animals comparable to Weigert's work in the human. In studies of animal brains there has been a tendency to be misled by a too rigid view of normality. Many changes

physiologist. In the epochal struggle between the two principles of on the one hand massive fertility combined with an enormous mortality in offspring (as, for instance, with fishes) and the opposite one of a lower mortality combined with greater parental care and often an associated delay in individual development, the latter principle would have seemed to be winning the day were it not for the impressive recrudescence of unicellular organisms and their pathological attacks on larger creatures. It has long been recognized that the human species was the supreme example of this second principle, which indeed may now be in the course of being carried to a dangerous extreme through the inordinate postponement of reproduction leading to a critical infertility.

In the mental field what is called the pleasure-pain principle—the search for pleasure and the avoidance of pain—is, if not all-embracing, of much more comprehensive scope than psychologists used to think. Freud has linked it with the Fechner stability principle of maintaining tension within certain definite limits and Wilbur[1] has recently correlated it with the more modern biological conception of "steady states". Some years ago Ferenczi[2] published a stimulating, though unequal, work in which he proposed to extend these conclusions from the mental field to the physical, and to found a new department of knowledge which he termed "Bio-analysis". The point that concerns us here is whether the functioning of individual organs and cells is determined solely by criteria of biological advantage, as is generally assumed, or whether this has to contend with physical tendencies comparable to the pleasure-pain ones of the mental field. Brun and other biologists have produced evidence, chiefly among insects, which strongly supports the latter suggestion by citing extreme cases where organic search for pleasurable sensations has even overwhelmed other tendencies with most deleterious, or even fatal, results to the species concerned. It is a thought that, even on the practical plane, is well worthy of consideration by those whose work is concerned with animal life.

Dr. Dorothy S. Russell (*Summary*): Advances in the field of comparative neuropathology follow two lines: (*a*) Observation of naturally occurring diseases in animals and comparison with human disease. (*b*) Experimental attempts to reproduce in laboratory animals the diseases recognized in human subjects.

The main branches in which studies have been made, and in which further progress is desirable are:—

(1) *Developmental abnormalities.*—The geneticist has a considerable contribution to make in the study of congenital malformations (*see* Grüneberg, 1944), and observations on such maldevelopments as familial cerebellar hypoplasia in Hereford calves (Innes, Russell and Wilsdon, 1940) may help to throw light on kindred affections in man.

(2) *Trauma.*—Studies in this branch have been mainly confined to experimental observations on concussion, and the healing of wounds in various circumstances.

(3) *Degenerations.*—The recent work of Weston Hurst (1942) on the demyelinations following the experimental use of different poisons suggests a new means of investigating this problem. At the same time the part played by copper in the ætiology of swayback in lambs, and observations on nervous distemper in dogs (Hurst, 1943), necessitates the retention of a wide view in this connexion.

(4) *Virus diseases.*—The histological reaction of the nervous system to known virus infections constitutes a separation between these inflammations and disseminated encephalomyelitis of a demyelinating character. Recent work on anterior poliomyelitis (Howe and Bodian, 1942) has led to a revision of our theories concerning the port of entry of the virus in human disease. and provides a striking instance of the dangers attached to the drawing of close analogies between the results of animal experimentation and disease in man

(5) *Intoxications.*—The growth of industry entails an increasing toll of occupational diseases. In the elucidation of these the experimental method finds an important place. An illustration is provided by an outbreak of poisoning by methyl mercury iodide in an East-End factory (Hunter, Bomford, and Russell, 1940), in which the victims showed gross nervous involvement.

(6) *Vitamin deficiencies* affecting the nervous system have been less extensively studied than in some other systems of the body. The results are somewhat equivocal. Thus the precise relationships between vitamin A deficiency and degeneration of nerve fibres, both in peripheral nerves and in central tracts, are still uncertain. The primary effect according to Mellanby (1941) is upon the bones. There is greater unanimity concerning vitamin B, deprivation of which leads to peripheral neuritis, also degeneration of the

[1]Wilbur, "Some Problems presented by Freud's Life-Death Instinct Theory", *American Imago*, 1941, 2, pp. 134 209.
[2]Ferenczi, Versuch einer Genitaltheorie, 1924, Vienna.

spinal roots and tracts within the cord. Of particular interest is the condition known as Wernicke's encephalopathy, which is now known to be due to a deficiency of this vitamin.

(7) *Tumours.*—Spontaneous neoplasms of the C.N.S. in animals may be commoner than is supposed. Recently, in the U.S.A., the experimental introduction into the brains of mice of pellets containing methyl cholanthrene. and more recently benzpyrene, has induced the growth of various meningeal and glial tumours.

(8) *Therapeutic trials.*—No account of animal experimentation would be complete without mentioning the trial of new · therapeutic agents, including various antibacterial substances. Experiments on the brain with compounds such as the acridine antiseptics, sulphonamide and penicillin have been helpful in the treatment of wounds involving the brain and meninges. It should be obligatory that· any therapeutic agent, whether chemical or physical, should be submitted to such tests before being tried on the human body.

REFERENCES
GRÜNEBERG, H. (1944) *Proc. Roy. Soc. Med.*, **37**, 125.
HOWE, H. A., and BODIAN, D. (1942) Neural Mechanisms in Poliomyelitis. , London.
HUNTER, D., BOMFORD, R. R., and RUSSELL, D. S. (1940) *Quart. J. Med.*, **9**, 193.
HURST, E. W. (1942) *Austral. J. Exp. Biol. and Med. Sci.*, **20**, 297.
——, COOK, B. T., and MELVIN, P. (1943) *Austral. J. Exp. Biol. and Med. Sci.*, **21**, 115.
INNES, J. R., RUSSELL, D. S., and WILSDON, A. J. (1940) *J. Path. Bact.*, **50**, 455.
MELLANBY, E. (1941) *J. Physiol.*, **99**, 467.

Dr. J. R. M. Innes (*Veterinary Research Laboratories, Wilmslow*): The purpose of the comparative study of diseases is not solely to shed light on human problems because animal studies have their intrinsic biological and utilitarian worth. A study of human diseases can be used for elucidation of animal problems for the simple reason that the fundamental principles of pathology were evolved originally by studies of human diseases and have since served as a basis for all veterinary work.

There is no real borderline between animal and human pathology and such differences which do exist are more apparent than real.

The medical worker begins with the advantage that there is more known about the human nervous system from all angles—anatomy, embryology, physiology and pathology —than the animal. An orderly system of classification of human nervous diseases has been built up, the scope of which increases as more knowledge is gained of the central nervous system as a functional organ. In the case of chronic progressive and relapsing conditions years may pass between disease inception and death. In such chronic diseases (of which there are many where experimental transmission is not yet possible) the human neurologist may have to be content with studying the end stages of a burnt-out process. The initial lesion must then be deduced· or guessed at, and in the search for ætiological explanation any causal agent may have disappeared from the scene of damage. There are a number of human nervous diseases in which such a stage has been reached and it is here that animal studies might be most profitably used.

On the animal side there is a contrast between the amount of investigation which has· been done on the comparative anatomy, physiology and histology (using the monkey, cat, dog and rat as type animals) and that on the comparative pathology of the central nervous system. Veterinary research workers have taken to a study of diseases of the animal nervous system often by accident with perhaps one or two outstanding exceptions, the most notable of which is work on animal virus encephalitides, which has contributed greatly to an understanding of encephalitis and the neurotropic viruses in man.

Accurate clinical· diagnosis of ·animal nervous diseases is difficult simply because the symptoms can only be objective in character. We do not yet possess data, which could only accrue by detailed examinations of the nervous system of large numbers of different animals nor do we know as yet to what extent the obscurer nervous disorders of man occur in animals. Sporadic nervous disorders have not been studied very much and there must be many non-fatal diseases of animals with nervous manifestations during life which are missed and which must remain unexplained on a pathological basis. Systematic investigations of the state of the central nervous system in general animal disease have not been made. Modern neuropathological technique is only beginning to be used in the veterinary field.

Much is known on the structure and course of the fibre tracts in certain animal species, e.g. dog, cat, monkey and rat, although little in the cow, sheep and horse and only fragmentary data concerning the finer nature of pathological processes of animals as a whole. There have been no comparable systematic studies of the distribution of glial cells in animals comparable to Weigert's work in the human. In studies of animal brains there has been a tendency to be misled by a too rigid view of normality. Many changes

in nerve cells in the animal brain have been described which might be devoid of any pathological significance; the appearances of vessel walls and significance of hyperæmia are often misconstrued; artificial alterations seem to be produced more easily. The reaction of the brain to pathogenic causes in man appears to be limited for we know that similar lesions can be produced by different agencies although perhaps in different locations. The brains of animals cannot be expected to behave in the same way when exposed to the same circumstances; comparative pathology, therefore, must seek to discover why these differences exist. There are many diseases of the nervous system of man (e.g. certain vascular disorders, aneurysms, the congenital and heredo-familial ataxias, the lipoidoses, amaurotic familial idiocy, the pre-senile dementias, tuberose sclerosis) which have so far not been described in animals.

There is much to be gained by comparative studies of the nervous system in animals based on the many lessons already learnt in human neuro-anatomy, histology and pathology.

The scope is wide in all directions and a few examples of types of conditions which have particularly interested me in the past are given below.

Embryology and malformations.—Studies of malformations are largely a question of embryology. The pioneer work and establishment of comparative embryology by men such as Müller, Baer, His and Kölliker was of fundamental importance because until their work on the germ layers a proper understanding of organogenesis and histogenesis was impossible. Flechsig and Langworthy indicated that myelination was a reflex of the onset and criterion of function of certain fibre systems, although too much reliance cannot be placed on myelination as such a criterion because of the variation in behaviour of some animals at birth which possess varying degrees of central myelination (cf. kittens and lambs). The demyelination diseases are an important group, and before any real understanding is obtained of the anatomic lesion itself we require more facts about myelin formation, development, and relation to function. Comparative studies of the behaviour of such conditions as swayback in lambs might well be correlated with physiological and embryological work—Barcroft has shown the lamb embryo will display mass movement if touched on the nose with a glass rod as early as the thirty-sixth day. There is then a precocious development of the nervous system in lambs, a fact which in itself would throw doubt on the view that myelination of tracts determines the onset of function.

At a recent meeting of this Section Grüneberg in his paper on animal genetics mentioned a large number of malformations in laboratory animals which were capable of study on genetical grounds. Many of these in domestic animals are lethal or sublethal and seem to have some genetical background. As Grüneberg has said they are experiments performed by nature and any insight into such processes is of value for the understanding of the working of the human body in health and disease.

Pigmentations.—Conditions such as this are non-lethal but they are biological phenomena, and we must seek to understand why there is such a variation in the occurrence and distribution in the various animal species as compared with man. For example, melanin pigmentation of the cells of the *substantia nigra* has been said to be specific for man although Scherer showed that it occurred in adult anthropoids. An explanation of this pigmentation cannot be divorced from that of the problem of melanin in general and its relationship to pigmented tumour formation inside and outside the central nervous system. In some animals, cows and sheep, melanin pigmentation is found normally in the central nervous system (mostly pial) with a frequency and degree rarely found in man. The cause is unknown and it would seem that it is an abnormal increase of chromatophores constantly present in the ovine and bovine meninges rather than as a heterotopic phenomenon.

The occurrence of iron pigmentation or siderosis is another peculiar pathological manifestation which seems to vary from animal to animal. Hurst, for example, showed that iron in association with calcium is a frequent finding in the vessels of the *globus pallidus* of horses while others have recorded the same condition in a *nucleus dentatus*. This was comparable to the human condition, the deposits lying either in the media or adventitia or both; in Hurst's cases there were no signs of generalized vascular disease nor was the condition related to that responsible for death. Similar appearances have been seen in monkeys but not in animals such as guinea-pigs, rabbits, mice, rats or dogs; it might, therefore, be a phenomenon of advancing life in the higher animals alone.

Demyelination diseases.—Broadly speaking one can divide this group of diseases into (1) a type associated with certain post-infective virus states, (2) a type associated with toxic conditions, and (3) a type which appears to be more idiopathic, such as disseminated sclerosis and Schilder's disease, the cause of which is unknown. Until the identification

of swayback in lambs there had been no pathological counterpart to any of this latter group in the lower animals apart from the isolated cases of Schilder's disease observed in monkeys. This group, therefore, contained good examples of diseases which, after having had a full weight of medical investigation thrown upon them without much result regarding ætiology, had reached a stage when the medical worker must remain content to study only static end stages. Experimentally a large number of substances have now been shown to be capable of causing demyelination. The most interesting results have been those of Hurst who used cyanide and sodium azide as a demyelination agent. Hurst showed a continuous series of lesions resulting from cyanide poisoning with cortical necrosis at one extreme and demyelination at the other. He stated that if we regard the white matter as possessing a poor capacity to recuperate from a number of relatively minor insults, which do not damage the grey matter, you may either get necrosis or demyelination according to their intensity. He drew attention to the similarity of the cyanide lesions in the experimental monkey to the spontaneous equine leuco-encephalitis (cornstalk disease) occurring in America, believed to be due to a toxic factor in damaged fodder.

The symptoms of swayback are mainly a spastic paralysis varying in degree according to extent of damage in the C.N.S. while the lesion is essentially a bilateral cerebral demyelination with degeneration of the motor paths. Certain stages resemble the anatomic picture of Schilder's disease in infants. The disease was shown to be somehow bound up with a deficiency of copper occurring in pregnant ewes but affecting only the myelin of the developing lamb. It was shown that the disease in lambs could be prevented by feeding Cu to the pregnant ewes. Whether or not further studies of this condition will help to elucidate the ætiology of the idiopathic human demyelination disorders remains to be seen. For the first time an association was shown between a physiological function of copper and myelin metabolism. Although we do not as yet understand the pathogenesis of this disease in lambs and why the lack of copper causes myelin degeneration, we should at least consider the possibility of trace elements being involved in the demyelination disorders of man. Several reports of conditions in human children have now appeared in the literature indicating that there may be a more exact human counterpart than the anatomical entity of Schilder's disease itself. Cases have now been recorded by four different authors in young children in some of which the disease has been antenatal in origin and in which the pathological findings more closely resembled the lamb cases. The suggestion has been made that many more may have occurred and been described, but lie buried in the literature under titles that give no true indication of the nature of the process, e.g. the case of polyporencephaly by Brocher.

I have tried to indicate broadly but briefly what the scope of comparative neuropathology is but it differs little from that of comparative pathology at large except in so far as it is a highly specialized branch of medicine. Pathology itself deals with investigations of the nature of disease, and the final explanation of any disease process must embrace that type of disease in its totality as it is seen in man and animals. Pathology is no different from the other biological sciences in which comparative studies have been successfully used and it is wrong to regard parallel conditions in man and animals as entities occupying watertight categories. Medicine as a whole cannot fail to profit if a broad view is taken. This is the plain teaching of comparative pathology free from theory and as envisaged by John Hunter himself.

Dr. W. S. Gordon : It was with great interest that I listened to Dr. Dorothy Russell's remarks that in poliomyelitis the olfactory lobes may be free from infection and that the natural route of infection is possibly *via* the alimentary canal. This observation opens up a wide field of inquiry because control of the disease depends largely on a sound knowledge of the path of infection in the naturally occurring disease.

Louping-ill is in many respects analogous to poliomyelitis,[1] it is an encephalomyelitis of sheep characterized by cerebellar ataxia and disorder of brain and spinal cord functions lasting a few days in acute cases to weeks of lingering illness. In chronic infections paralysis of one or more limbs may result. In the early phase of the investigation of this disease we believed that the infection was from the outset and exclusively an infection of nerve tissues. We found later that the virus multiplied in the first instance elsewhere than in the nervous system, that the blood became infective during the febrile period which precedes symptoms of central nervous system involvement, that the tick *Ixodes*

[1] GORDON, W. S. (1934) *Proc. R. Soc. Med.*, 27, 701.

in nerve cells in the animal brain have been described which might be devoid of any pathological significance; the appearances of vessel walls and significance of hyperæmia are often misconstrued; artificial alterations seem to be produced more easily. The reaction of the brain to pathogenic causes in man appears to be limited for we know that similar lesions can be produced by different agencies although perhaps in different locations. The brains of animals cannot be expected to behave in the same way when exposed to the same circumstances; comparative pathology, therefore, must seek to discover why these differences exist. There are many diseases of the nervous system of man (e.g. certain vascular disorders, aneurysms, the congenital and heredo-familial ataxias, the lipoidoses, amaurotic familial idiocy, the pre-senile dementias, tuberose sclerosis) which have so far not been described in animals.

There is much to be gained by comparative studies of the nervous system in animals based on the many lessons already learnt in human neuro-anatomy, histology and pathology.

The scope is wide in all directions and a few examples of types of conditions which have particularly interested me in the past are given below.

Embryology and malformations.—Studies of malformations are largely a question of embryology. The pioneer work and establishment of comparative embryology by men such as Müller, Baer, His and Kölliker was of fundamental importance because until their work on the germ layers a proper understanding of organogenesis and histogenesis was impossible. Flechsig and Langworthy indicated that myelination was a reflex of the onset and criterion of function of certain fibre systems, although too much reliance cannot be placed on myelination as such a criterion because of the variation in behaviour of some animals at birth which possess varying degrees of central myelination (cf. kittens and lambs). The demyelination diseases are an important group, and before any real understanding is obtained of the anatomic lesion itself we require more facts about myelin formation, development, and relation to function. Comparative studies of the behaviour of such conditions as swayback in lambs might well be correlated with physiological and embryological work—Barcroft has shown the lamb embryo will display mass movement if touched on the nose with a glass rod as early as the thirty-sixth day. There is then a precocious development of the nervous system in lambs, a fact which in itself would throw doubt on the view that myelination of tracts determines the onset of function.

At a recent meeting of this Section Grüneberg in his paper on animal genetics mentioned a large number of malformations in laboratory animals which were capable of study on genetical grounds. Many of these in domestic animals are lethal or sublethal and seem to have some genetical background. As Grüneberg has said they are experiments performed by nature and any insight into such processes is of value for the understanding of the working of the human body in health and disease.

Pigmentations.—Conditions such as this are non-lethal but they are biological phenomena, and we must seek to understand why there is such a variation in the occurrence and distribution in the various animal species as compared with man. For example, melanin pigmentation of the cells of the *substantia nigra* has been said to be specific for man although Scherer showed that it occurred in adult anthropoids. An explanation of this pigmentation cannot be divorced from that of the problem of melanin in general and its relationship to pigmented tumour formation inside and outside the central nervous system. In some animals, cows and sheep, melanin pigmentation is found normally in the central nervous system (mostly pial) with a frequency and degree rarely found in man. The cause is unknown and it would seem that it is an abnormal increase of chromatophores constantly present in the ovine and bovine meninges rather than as a heterotopic phenomenon.

The occurrence of iron pigmentation or siderosis is another peculiar pathological manifestation which seems to vary from animal to animal. Hurst, for example, showed that iron in association with calcium is a frequent finding in the vessels of the *globus pallidus* of horses while others have recorded the same condition in a *nucleus dentatis*. This was comparable to the human condition, the deposits lying either in the media or adventitia or both; in Hurst's cases there were *no* signs of generalized vascular disease nor was the condition related to that responsible for death. Similar appearances have been seen in monkeys but not in animals such as guinea-pigs, rabbits, mice, rats or dogs; it might, therefore, be a phenomenon of advancing life in the higher animals alone.

Demyelination diseases.—Broadly speaking one can divide this group of diseases into (1) a type associated with certain post-infective virus states, (2) a type associated with toxic conditions, and (3) a type which appears to be more idiopathic, such as disseminated sclerosis and Schilder's disease, the cause of which is unknown. Until the identification

Dr. W. H. Andrews dealt with the effects of intoxications on the nervous system of animals, and to the interesting differences in the symptoms which may be shown even by closely related species of animals when affected by a particular drug; e.g. the great difference between dogs and cats in their reaction to morphine.

He also dealt briefly with the effects on animals of snake venoms, and the variety of symptoms which might result from stimulation or depression of the nervous system in varying degrees of intensity and over very localized or more diffuse areas. He mentioned a tendency of affected equine and bovine animals to push with the head against walls or trees, a tendency shown by these animals very commonly and more markedly in a number of forms of plant poisoning. The occurrence of violent vomiting and retching in sheep affected by cobra venom was a symptom of great interest, having regard to the fact that the vomiting mechanism appeared to be very poorly developed in these animals. Sheep were rarely seen to vomit, even after the ingestion of large and fatal doses of an irritant poison.

Some of the most interesting symptoms referable to the nervous system of animals were to be seen in certain forms of plant poisoning. There was a group of intoxications of this kind in which the effects developed comparatively slowly and visible symptoms were shown only after a considerable period of latency. For example, in cases of poisoning by one species of *Senecio*, the first symptoms of illness might be noticeable as long as ninety-six days, and perhaps longer, after the last occasion on which the animal had had any opportunity of ingesting the plant. In this group of intoxications the slow development would obviously allow time for the appearance of definite lesions in the nervous system; no such lesions had been described but they might well exist, for he did not think that in any of these conditions the nervous system had been submitted to the full and specialized examination that was required. In all members of this group, however, there were well-marked lesions of the liver; in some instances this took the form of a fatty degeneration and in others there were necrosis and cirrhosis.

As a particularly interesting example of this group Dr. Andrews briefly described an intoxication caused by the ingestion of *Matricaria nigellæfolia*, a common weed of low-lying, damp areas in Natal. Horses, sheep, goats and pigs could apparently eat this plant with impunity. The intoxication appeared only in cattle and for its development it seemed necessary for the plant to be eaten for at least some days. No symptoms were seen until at least three weeks had elapsed, and they might appear as long as six weeks after the last occasion on which the plant was eaten. The actual course of visible illness varied from about a week (exceptionally three or four days) to many weeks, and the case mortality was usually very high.

In this condition the nervous system was profoundly affected. In the earlier stages the animal was very restless and later, during the active phases, it generally showed signs of excitement and sometimes, after a heavy fall, of fear. In many cases consciousness seemed not to be lost or greatly disturbed until the onset of the final stage of coma, but in very acute cases there were periods of what appeared to be delirium or even mania.

Inco-ordination of movement was a well-marked feature of subacute cases, and in the earliest stages it seemed often to affect particularly the control of the lips and tongue, so that food and especially water, could not be taken into the mouth, although swallowing of material placed in the mouth could still be effected. In connexion with the limbs, an initial slight tendency to stumble developed into an uncertain, staggering gait, and the assumption of abnormal and often strange postures. Muscular contractions were a prominent feature of all acute cases. At first there was commonly a mere fibrillation or tremor, often very localized, but either gradually or very rapidly the contractions became stronger and more diffuse, until there were violent spasms, clonic or tonic, and ultimately general convulsions. During the active phases the reflex irritability was greatly increased; as the disease progressed, the responses to stimuli (pain, tactile, auditory) became more violent and, especially with repetition of stimulation, more diffuse.

There were three features of this condition that were of particular interest. In the first place, no definite signs of paralysis were seen in most cases of *Matricaria* intoxication, but in some cases, and particularly in slowly developing cases, arising from the ingestion of relatively small amounts of the plant, the animals showed a well-marked paresis or paralysis of the extensors of the forelimb. At first the animal was unable to extend the metacarpophalangeal joint, and later, in some cases, the carpal joint also. This condition, which was never seen to affect the hindlimb, might be compared with the "wrist-drop" of chronic lead poisoning in man.

In the second place, the muscular contractions were often rhythmic in a striking degree. Clonic spasms affecting the limbs were often quite irregular, but sometimes showed a regular rhythm, and the phenomenon was most frequently seen in connexion

ricinus was a vector of the virus and that the disease could be readily prevented by the subcutaneous inoculation of susceptible sheep with a formalinized 10% saline suspension of infected brain and spinal cord tissues. This vaccine, although capable of blocking either the naturally occurring disease or a test dose of virus subcutaneously, failed to immunize the central nervous system against a dose of virus introduced intracranially.

It is in a field such as this, the study of analogous diseases in man and animals, that the comparative method has considerable uses. At the present time the medical immunologist may believe that to produce immunity to poliomyelitis it is necessary to immunize the central nervous system. That would be true if the virus multiplies in nerve tissues only, but if it has a preliminary phase of activity in tissues outside the nervous system then, as with louping-ill, the production of immunity might be simple. Similarly, in louping-ill the number of subclinical cases with blood infection are far in excess of frank cases with central nervous system involvement and consequently in the perpetuation and spread of this disease subclinical infections have a more important role than definite clinical cases. If the same, as is probable, is true in poliomyelitis it explains why such a large percentage of the adult human population has neutralizing antibody for the virus of poliomyelitis, and provides an explanation as to how the virus bridges the gap between two widely separated outbreaks. Rivers observed that man is susceptible to louping-ill, and we have found virus-neutralizing antibody in the serum of ten laboratory workers who had been in intimate contact with the virus, and illness, sometimes of a serious nature, had occurred in these individuals prior to the serum examinations. More recently D. R. Wilson of Moredun Institute has isolated the virus from the blood of two laboratory workers during an illness suspected to be due to louping-ill. In one of these the blood was inoculated both into mice intracerebrally and chick embryo medium and it was only by the latter method that the virus was recovered. It is also probable that natural cases of louping-ill occur in man since a serum sample, sent to us by Dr. J. Smith of Aberdeen from a sheep farmer suspected to have been affected by the disease, was found to contain antibody capable of neutralizing the virus.

During the investigation of louping-ill another and distinct tick-borne disease was discovered; this disease was named tick-borne fever. It is characterized by an incubation period of about four days followed by a febrile reaction which lasts about ten days. The infective agent is a rickettsia-like organism which can be observed in the cytoplasm of the granular leucocytes. It is not a fatal disease but it aggravates the harmful effects of a louping-ill infection and since, in nature, it is liable to occur concurrently with that disease a comparison was made of the type of infection that developed in a group of sheep infested with ticks known to harbour the virus of louping-ill only and a group which were infested with fellow ticks and simultaneously infected with tick-borne fever. The evidence indicated that the virus of louping-ill was more liable to gain access to the central nervous system when the combined infections were produced.

Another disease of sheep of unknown ætiology named "scrapie" has been recognized in Northern Europe for the last 200 years. It is a neurosis, characterized by symptoms of intense and progressive pruritis, progressive asthenia and locomotor inco-ordination. The course, which usually extends over several months, invariably terminates fatally. Louping-ill prophylactic vaccine comprises a formalinized (0·35% of 40% formaldehyde) emulsion of brain, spinal cord and spleen, obtained from sheep artificially infected with louping-ill. Evidence has been obtained that several hundred sheep out of 14,000 inoculated in 1935 with one batch of this vaccine became affected with scrapie in 1937 and 1938, while scrapie did not develop in 28,000 sheep inoculated with different batches of vaccine produced in the same year. It has since been found that certain yearling sheep used in the preparation of the contaminated batch of vaccine were, at the time, actually affected with scrapie although they showed no clinical symptoms. As a result of this accident, we now possess evidence, which has since been confirmed, that: (a) the infective agent is present in the brain, spinal cord and spleen; (b) it can withstand 0·35% of formalin; (c) it can be transmitted by subcutaneous inoculation; (d) the incubative period may extend to at least two years.

It has since been found that the incubation period can be reduced to seven months by intracerebral inoculation. Brownlee (1940) concluded that vacuolation of the nerve cells of the medulla and/or spinal cord is constantly present in scrapie. This has been confirmed by Holman and Pattison (1943) who further observed that the distribution of vacuolated cells in the medulla oblongata is selective for certain groups of cells, notably the reticular formation, medial vestibular and lateral cuneate nuclei.

REFERENCES

BROWNLEE, A. (1940) *Vet. J.*, 96, 254.
HOLMAN, H. H., and PATTISON, I. H. (1943) *J. comp. Path.*, 53, 231.

Dr. W. H. Andrews dealt with the effects of intoxications on the nervous system of animals, and to the interesting differences in the symptoms which may be shown even by closely related species of animals when affected by a particular drug; e.g. the great difference between dogs and cats in their reaction to morphine.

He also dealt briefly with the effects on animals of snake venoms, and the variety of symptoms which might result from stimulation or depression of the nervous system in varying degrees of intensity and over very localized or more diffuse areas. He mentioned a tendency of affected equine and bovine animals to push with the head against walls or trees, a tendency shown by these animals very commonly and more markedly in a number of forms of plant poisoning. The occurrence of violent vomiting and retching in sheep affected by cobra venom was a symptom of great interest, having regard to the fact that the vomiting mechanism appeared to be very poorly developed in these animals. Sheep were rarely seen to vomit, even after the ingestion of large and fatal doses of an irritant poison.

Some of the most interesting symptoms referable to the nervous system of animals were to be seen in certain forms of plant poisoning. There was a group of intoxications of this kind in which the effects developed comparatively slowly and visible symptoms were shown only after a considerable period of latency. For example, in cases of poisoning by one species of *Senecio*, the first symptoms of illness might be noticeable as long as ninety-six days, and perhaps longer, after the last occasion on which the animal had had any opportunity of ingesting the plant. In this group of intoxications the slow development would obviously allow time for the appearance of definite lesions in the nervous system; no such lesions had been described but they might well exist, for he did not think that in any of these conditions the nervous system had been submitted to the full and specialized examination that was required. In all members of this group, however, there were well-marked lesions of the liver; in some instances this took the form of a fatty degeneration and in others there were necrosis and cirrhosis.

As a particularly interesting example of this group Dr. Andrews briefly described an intoxication caused by the ingestion of *Matricaria nigellæfolia*, a common weed of low-lying, damp areas in Natal. Horses, sheep, goats and pigs could apparently eat this plant with impunity. The intoxication appeared only in cattle and for its development it seemed necessary for the plant to be eaten for at least some days. No symptoms were seen until at least three weeks had elapsed, and they might appear as long as six weeks after the last occasion on which the plant was eaten. The actual course of visible illness varied from about a week (exceptionally three or four days) to many weeks, and the case mortality was usually very high.

In this condition the nervous system was profoundly affected. In the earlier stages the animal was very restless and later, during the active phases, it generally showed signs of excitement and sometimes, after a heavy fall, of fear. In many cases consciousness seemed not to be lost or greatly disturbed until the onset of the final stage of coma, but in very acute cases there were periods of what appeared to be delirium or even mania.

Inco-ordination of movement was a well-marked feature of subacute cases, and in the earliest stages it seemed often to affect particularly the control of the lips and tongue, so that food and especially water, could not be taken into the mouth, although swallowing of material placed in the mouth could still be effected. In connexion with the limbs, an initial slight tendency to stumble developed into an uncertain, staggering gait, and the assumption of abnormal and often strange postures. Muscular contractions were a prominent feature of all acute cases. At first there was commonly a mere fibrillation or tremor, often very localized, but either gradually or very rapidly the contractions became stronger and more diffuse, until there were violent spasms, clonic or tonic, and ultimately general convulsions. During the active phases the reflex irritability was greatly increased; as the disease progressed, the responses to stimuli (pain, tactile, auditory) became more violent and, especially with repetition of stimulation, more diffuse.

There were three features of this condition that were of particular interest. In the first place, no definite signs of paralysis were seen in most cases of *Matricaria* intoxication, but in some cases, and particularly in slowly developing cases, arising from the ingestion of relatively small amounts of the plant, the animals showed a well-marked paresis or paralysis of the extensors of the forelimb. At first the animal was unable to extend the metacarpophalangeal joint, and later, in some cases, the carpal joint also. This condition, which was never seen to affect the hindlimb, might be compared with the "wrist-drop" of chronic lead poisoning in man.

In the second place, the muscular contractions were often rhythmic in a striking degree. Clonic spasms affecting the limbs were often quite irregular, but sometimes showed a regular rhythm, and the phenomenon was most frequently seen in connexion

with an antero-posterior movement of the ears; this ear movement, which often appeared at a very early stage of the disease, was extremely rapid but appeared to be very regular. In one case observed by the speaker, the animal showed an alternate extension and flexion of the head on the neck which produced a nodding or rocking motion of the head. This movement was strangely regular, with a rhythm of about thirty cycles to the minute, and it occurred in bouts lasting from about five to fifteen minutes. At the commencement of each bout, the contractions were very strong and the head moved through a wide arc, but the movements gradually decreased in amplitude until they died away. The periods of quiescence between the bouts were of variable length, but renewed nodding could be provoked by any form of tactile, painful or auditory stimulation.

The third feature of special interest was a tendency of the affected animals to push with the head against some immovable object such as a wall or tree. This was shown at some stage in all or practically all cases, and it was so pronounced a feature of *Matricaria* intoxication that the condition was known popularly as "pushing disease", although this pushing was sometimes seen in animals affected by cobra venom and it was commonly observed in cases of other conditions, including intoxications due to a number of plants other than *Matricaria*. The action varied from a mere resting of the head on or against the rigid object to a very violent pushing, sometimes accompanied by stepping movements of the legs; it was sometimes so violent that, when the head slipped from or along the rigid object, the animal might turn a somersault on to the back. From observation it appeared that in the earlier stages or milder forms the pushing with the head might be a conscious, purposive act, from which the animal seemed to derive some satisfaction and from which it would immediately desist when approached. At a later stage, and in its more violent manifestations, it was almost certainly not a conscious but a reflex act which could be stimulated or intensified by almost any form of sensory stimulus. Some of the evidence suggested that in this more violent form the animal was impelled, not so much to push against objects but rather to move forward in a more or less straight line, and that it would wander forward, sometimes for miles, until its further progress was checked by some rigid object in its path. There seemed to be some reason for thinking that this behaviour of the animal might represent a form of "stepping reflex" and that this, as well as the rhythmic movements previously mentioned, might result from stimulation of motor centres by a stream of nearly balanced, antagonistic impulses.

Cases of *Matricaria* intoxication showed post mortem some hepatic degeneration, and it was perhaps of interest to compare some of the manifestations of this condition with the restlessness, muscular spasms and delirium that might be seen in man in cases of acute yellow atrophy.

Dr. C. L. Oakley said that he was surprised that Hurst had been so successful in recovering distemper virus from cases of encephalomyelitis in dogs; Perdrau and Pugh had been completely unsuccessful, and so had he. As distemper virus *could* be recovered readily from a form of cerebral distemper showing degeneration of nerve cells and neuronophagy, he suspected that more than one disease was involved, and that distemper merely activated another latent infection.

[June 21, 1944]

DISCUSSION ON THE LIMITATIONS AND USES OF THE COMPARATIVE METHOD IN MEDICINE

V. Comparative Psychology and Animal Behaviour

Dr. C. S. Myers (*The comparative study of instincts*): Dr. Myers drew attention to the relative neglect of this study until recently, and to its great importance for the better understanding of the evolution of instincts. He urged the need for observing instincts arising or disappearing through mutations or under other conditions, e.g. the transitory appearance of phylogenetically old instincts during ontogeny. He drew attention to the distinctive characters of instincts at different levels of animal life, especially to the degree to which in man intelligence has usurped the functions of specific inherited behaviour, while at the same time the instinctive nature of the general "determining direction" of behaviour is preserved and is clearly recognizable. Finally, he mentioned the taxonomic significance of similar instinctive behaviour, hitherto virtually disregarded by systematists.

This he exemplified by Heinroth's work on the distribution of two types of "scratching" in birds and by Lorenz's work on the distribution of the "chin-lift" and "pursuit" responses among mallards, widgeons, gadwalls, &c. He also pointed out how two widely different organisms, such as termites and ants, may develop an elaborate, closely similar, social organization involving the development of closely similar instincts.

(To be published in full in the *British Journal of Psychology*, 1945.)

Dr. W. H. Thorpe (*The types of animal learning and their relation to the problem of instinct*): Dr. W. H. Thorpe classified animal learning into: Habituation, Associative Learning (Conditioning and Trial and Error), Latent Learning, Insight Learning and Imprinting, the first and last of which were particularly related to the problem of Instinct. Habituation was a process which ensured that the animal did not waste time and energy in continued response to a large variety of generalized mild shock and "warning" stimuli when these proved not to be followed by injurious results. By its means the animal learnt to ignore those mild stimuli which proved after all to be harmless or of no significance. Imprinting was a special type of learning, occurring primarily in animals which do not recognize their own species instinctively. By its means the young animal came to respond to those highly elaborate patterns of stimuli which were characteristic of its species. Imprinting thus resulted in the acquisition of the biologically "right" object of social reactions. Imprinting might thus act as a fine adjustment for certain complex instinctive responses or might entirely replace instinctive recognition of elaborate species patterns.

(To be published in full in the *Proceedings of the Linnean Society of London*, 1944, under the title "Some Problems of Animal Learning".)

Professor D. B. Johnstone-Wallace[1] and Captain Keith Kennedy[2] (*Grazing management practices and their relationship to the behaviour and grazing habits of cattle*): The principal objectives of the investigation were to determine: (1) The grazing habits of beef cattle during continuous periods of twenty-four hours when on pasture and receiving no supplementary feed. (2) The amount of pasture herbage consumed in twenty-four hours on pastures at various stages of growth and grazing. (3) The chemical composition of the herbage consumed. (4) The influence of methods of grazing management upon the production and chemical and botanical composition of pasture herbage.

METHODS OF PROCEDURE

Records were obtained of the behaviour of selected Aberdeen Angus and Hereford cows during continuous periods of twenty-four hours on excellent Kentucky blue-grass and wild white clover pastures of from three to seven acres. A map was made showing the path travelled by the cow and the time occupied in various performances during the day and night. The position of the cow was recorded in relationship to numbered stakes distributed throughout the field and time records were obtained with a stop watch.

Determinations of the amount of herbage consumed were made by mowing strips 40 feet long and 25 inches wide. The machine was set to cut to within one-half inch of the ground surface to simulate the observed grazing habits of the cattle under the conditions prevailing. From six to ten strips per acre were used to determine the amount of herbage present per acre. The strips were mowed immediately before the cattle were turned into the field and strips parallel to these were mowed at intervals of one to four days. The rate of growth of the herbage was measured by reclipping the original strips and by weekly mowings made on ungrazed plots of similar botanical composition in the adjoining field.

The weight and moisture content of the manure deposited was determined and the area covered by droppings was measured.

RESULTS

Grazing habits.—In twenty-four hours the average time spent in grazing was seven hours and thirty-two minutes of which approximately 60% was during the day and 40% during the night. It was estimated that only five hours were used in the actual gathering of herbage because of the time spent in walking short distances and in selecting herbage to be grazed. The time spent in chewing the cud averaged seven hours. The time

[1]Assistant Professor of Agrostology, Cornell University.
[2]New York Farmers' Pasture Research Fellow, Cornell University, now Captain, U.S. Army.

with an antero-posterior movement of the ears; this ear movement, which often appeared at a very early stage of the disease, was extremely rapid but appeared to be very regular. In one case observed by the speaker, the animal showed an alternate extension and flexion of the head on the neck which produced a nodding or rocking motion of the head. This movement was strangely regular, with a rhythm of about thirty cycles to the minute, and it occurred in bouts lasting from about five to fifteen minutes. At the commencement of each bout, the contractions were very strong and the head moved through a wide arc, but the movements gradually decreased in amplitude until they died away. The periods of quiescence between the bouts were of variable length, but renewed nodding could be provoked by any form of tactile, painful or auditory stimulation.

The third feature of special interest was a tendency of the affected animals to push with the head against some immovable object such as a wall or tree. This was shown at some stage in all or practically all cases, and it was so pronounced a feature of *Matricaria* intoxication that the condition was known popularly as "pushing disease", although this pushing was sometimes seen in animals affected by cobra venom and it was commonly observed in cases of other conditions, including intoxications due to a number of plants other than *Matricaria*. The action varied from a mere resting of the head on or against the rigid object to a very violent pushing, sometimes accompanied by stepping movements of the legs; it was sometimes so violent that, when the head slipped from or along the rigid object, the animal might turn a somersault on to the back. From observation it appeared that in the earlier stages or milder forms the pushing with the head might be a conscious, purposive act, from which the animal seemed to derive some satisfaction and from which it would immediately desist when approached. At a later stage, and in its more violent manifestations, it was almost certainly not a conscious but a reflex act which could be stimulated or intensified by almost any form of sensory stimulus. Some of the evidence suggested that in this more violent form the animal was impelled, not so much to push against objects but rather to move forward in a more or less straight line, and that it would wander forward, sometimes for miles, until its further progress was checked by some rigid object in its path. There seemed to be some reason for thinking that this behaviour of the animal might represent a form of "stepping reflex" and that this, as well as the rhythmic movements previously mentioned, might result from stimulation of motor centres by a stream of nearly balanced, antagonistic impulses.

Cases of *Matricaria* intoxication showed post mortem some hepatic degeneration, and it was perhaps of interest to compare some of the manifestations of this condition with the restlessness, muscular spasms and delirium that might be seen in man in cases of acute yellow atrophy.

Dr. C. L. Oakley said that he was surprised that Hurst had been so successful in recovering distemper virus from cases of encephalomyelitis in dogs; Perdrau and Pugh had been completely unsuccessful, and so had he. As distemper virus *could* be recovered readily from a form of cerebral distemper showing degeneration of nerve cells and neuronophagy, he suspected that more than one disease was involved, and that distemper merely activated another latent infection.

[June 21, 1944]

DISCUSSION ON THE LIMITATIONS AND USES OF THE COMPARATIVE METHOD IN MEDICINE

V. Comparative Psychology and Animal Behaviour

Dr. C. S. Myers (*The comparative study of instincts*): Dr. Myers drew attention to the relative neglect of this study until recently, and to its great importance for the better understanding of the evolution of instincts. He urged the need for observing instincts arising or disappearing through mutations or under other conditions, e.g. the transitory appearance of phylogenetically old instincts during ontogeny. He drew attention to the distinctive characters of instincts at different levels of animal life, especially to the degree to which in man intelligence has usurped the functions of specific inherited behaviour, while at the same time the instinctive nature of the general "determining direction" of behaviour is preserved and is clearly recognizable. Finally, he mentioned the taxonomic significance of similar instinctive behaviour, hitherto virtually disregarded by systematists

This he exemplified by Heinroth's work on the distribution of two types of "scratching" in birds and by Lorenz's work on the distribution of the "chin-lift" and "pursuit" responses among mallards, widgeons, gadwalls, &c. He also pointed out how two widely different organisms, such as termites and ants, may develop an elaborate, closely similar, social organization involving the development of closely similar instincts.

(To be published in full in the *British Journal of Psychology*, 1945.)

Dr. W. H. Thorpe (*The types of animal learning and their relation to the problem of instinct*): Dr. W. H. Thorpe classified animal learning into: Habituation, Associative Learning (Conditioning and Trial and Error), Latent Learning, Insight Learning and Imprinting, the first and last of which were particularly related to the problem of Instinct. Habituation was a process which ensured that the animal did not waste time and energy in continued response to a large variety of generalized mild shock and "warning" stimuli when these proved not to be followed by injurious results. By its means the animal learnt to ignore those mild stimuli which proved after all to be harmless or of no significance. Imprinting was a special type of learning, occurring primarily in animals which do not recognize their own species instinctively. By its means the young animal came to respond to those highly elaborate patterns of stimuli which were characteristic of its species. Imprinting thus resulted in the acquisition of the biologically "right" object of social reactions. Imprinting might thus act as a fine adjustment for certain complex instinctive responses or might entirely replace instinctive recognition of elaborate species patterns.

(To be published in full in the *Proceedings of the Linnean Society of London*, 1944, under the title "Some Problems of Animal Learning".)

Professor D. B. Johnstone-Wallace[1] and **Captain Keith Kennedy**[2] (*Grazing management practices and their relationship to the behaviour and grazing habits of cattle*): The principal objectives of the investigation were to determine: (1) The grazing habits of beef cattle during continuous periods of twenty-four hours when on pasture and receiving no supplementary feed. (2) The amount of pasture herbage consumed in twenty-four hours on pastures at various stages of growth and grazing. (3) The chemical composition of the herbage consumed. (4) The influence of methods of grazing management upon the production and chemical and botanical composition of pasture herbage.

METHODS OF PROCEDURE

Records were obtained of the behaviour of selected Aberdeen Angus and Hereford cows during continuous periods of twenty-four hours on excellent Kentucky blue-grass and wild white clover pastures of from three to seven acres. A map was made showing the path travelled by the cow and the time occupied in various performances during the day and night. The position of the cow was recorded in relationship to numbered stakes distributed throughout the field and time records were obtained with a stop watch.

Determinations of the amount of herbage consumed were made by mowing strips 40 feet long and 25 inches wide. The machine was set to cut to within one-half inch of the ground surface to simulate the observed grazing habits of the cattle under the conditions prevailing. From six to ten strips per acre were used to determine the amount of herbage present per acre. The strips were mowed immediately before the cattle were turned into the field and strips parallel to these were mowed at intervals of one to four days. The rate of growth of the herbage was measured by reclipping the original strips and by weekly mowings made on ungrazed plots of similar botanical composition in the adjoining field.

The weight and moisture content of the manure deposited was determined and the area covered by droppings was measured.

RESULTS

Grazing habits.—In twenty-four hours the average time spent in grazing was seven hours and thirty-two minutes of which approximately 60% was during the day and 40% during the night. It was estimated that only five hours were used in the actual gathering of herbage because of the time spent in walking short distances and in selecting herbage to be grazed. The time spent in chewing the cud averaged seven hours. The time

[1] Assistant Professor of Agrostology, Cornell University.
[2] New York Farmers' Pasture Research Fellow, Cornell University, now Captain, U.S. Army.

spent lying down averaged twelve hours, but this was divided into nine periods varying from less than one hour to more than six hours. The time spent in suckling the calf averaged forty-five minutes and this was divided into three periods of fifteen minutes each. The cows walked two and a half miles of which one half-mile was travelled during the night. They drank water once during the twenty-four hours. The average moisture content of the herbage consumed was 72%.

Amount of herbage consumed.—The cows showed a preference for immature leafy herbage of from four to five inches in height and it was apparent that the sense of smell was employed in determining the herbage selected. Herbage in the vicinity of areas where cattle droppings had been deposited was avoided.

An average of from 50 to 70 bites per minute were taken during the process of grazing, although occasionally 90 bites per minute were recorded. The cattle were observed to graze continuously without raising their heads from the ground for periods of up to forty minutes, although shorter periods were usual when selective grazing was much in evidence.

When the pasture averaged four to five inches in height and consisted of a dense sward of Kentucky blue-grass and wild white clover, the amount of herbage present per acre averaged 4,500 lb. green material containing 1,000 lb. dry matter. The amount consumed by beef cows averaging about 1,300 pounds live-weight was found to be 150 lb. green material containing 32 lb. dry matter.

After a few days of grazing when the amount of herbage present per acre had been reduced to 2,200 lb. green material containing 500 lb. dry matter, the amount consumed averaged 90 lb. green material containing 20 lb. dry matter.

After a further period of grazing had reduced the amount of herbage per acre to 1,100 lb. green material containing 250 lb. dry matter, the amount consumed was 45 lb. green material containing 10 lb. dry matter.

There was very little variation in the time spent in grazing and it was apparent that the animals made little attempt to increase the amount of herbage consumed under unfavourable conditions by working overtime.

When herbage was allowed to grow to a height of ten inches before the cattle were turned into a pasture, the amount of herbage present per acre was found to be approximately 5,000 lb. green material containing 1,200 lb. dry matter. The amount of herbage consumed by the cattle was 70 lb. green material containing 20 lb. dry matter. The protein content of such herbage was found to be 40% lower than that of herbage at a height of four to five inches, and the lignin content was higher.

Manure and urine deposited.—Dung was deposited approximately twelve times and urine nine times daily. The total weight of fresh dung averaged about 46 lb. daily and contained about 6¼ lb. dry matter. The area covered by dung daily was estimated to be approximately eight square feet. No record was obtained of the weight of urine deposited or of the amount of water the cows drank.

The influence of grazing management practices on pasture herbage.—This part of the investigation is still in progress with the object of determining the influence of grazing management practices upon the yield and botanical and chemical composition of the herbage of a Kentucky blue-grass and wild white clover pasture, over a period of several years. The data obtained in 1940 show that the percentage of wild white clover in the herbage was increased by frequent close clipping and that the plots cut to within one-half inch from the ground surface whenever the herbage reached a height of approximately four inches, gave a greater yield of dry matter and protein per acre than plots cut from six inches to one-half inch, eight inches to one-half inch, eight inches to two inches, six inches to four inches, six inches to two inches. four inches to two inches, once a year for hay, and twice a year for hay. Similar results were obtained in 1941 for yield of dry matter but the protein figures are not yet available.

Dr. Arthur Walton, *School of Agriculture, Cambridge* (*Comparative sexual behaviour of the male*): An animal's behaviour is, in very large measure, determined by anatomical structure. For example the male behaves as a male, not, primarily, because it is genetically different from the female, nor because it is sexually motivated by the male hormone, but principally because the male possesses genital organs of a specific structure and sensitivity situated in a certain region of the body. This is equally true of the female with which he mates. For example the cervix of the cow is long and rigid and its lumen narrow and tortuous. Fluid in bulk cannot pass through the cervix and spermatozoa find entrance to the uterus by their own motility. This determines that fertilization is most efficiently effected by the deposition of a small volume of highly concentrated semen

at the entrance to the cervix. In conformity with this the accessory glands of the bull are small and only a small volume of fluid is ejaculated. This small quantity can be deposited rapidly in the vagina by a single thrust of the bull's penis which is pointed and penetrates easily into the vagina. The ejaculatory reflex is elicited by the sensation of warmth to which the penis is particularly sensitive and ejaculation follows intromission almost immediately. With this rapid .completion of copulation is associated a correspondingly short preliminary sexual excitory courtship.

Quite a different pattern of behaviour is seen in the boar. The uterine horns of the sow are long. There is little constriction at the cervix. Semen in considerable volume can pass through and be conveyed by peristaltic contractions from the vagina to the ends of the uterine horns. To fit these conditions the boar has a much more protracted preliminary courtship, intromission is slow, the penis is not particularly sensitive to warmth and the ejaculatory reflex is not elicited by warmth so much as by the pressure of the peristaltic waves of the vagina. A large volume of semen is ejaculated in a succession of pulsations, the accessory glands being well developed. The whole process of copulation may last from 15 to 30 minutes. This comparison with the bull will illustrate how to a very large extent the pattern of sexual behaviour is correlated with anatomical structure.

Sexual reflexes are much more limited in number than one might at first suppose from the complexity of the mating pattern, but this complexity is due not so much to the number of reflexes as to the extent to which the basic unconditioned reflexes are conditioned by environmental stimuli acting through the various sense organs. The basic reflexes are probably not more than about four: the mounting reflex, the erection reflex, the exploratory reflex or reflex of intromission and the ejaculatory reflex. The mounting reflex has an extremely low and non-specific threshold, it appears very early in life before puberty and is not markedly sex specific. Appearance, smell and tactile sensations may, however, become conditioning stimuli to the mounting reflex. The erection reflex appears to depend upon mounting in the first instance and generally only succeeds it in point of time, but erection may become conditioned by various environmental associations and eventually can be elicited independently of mounting and may even precede it in point of time. The intromission reflexes, by which the penis is guided by trial and error into the vagina, do not appear to depend upon very specific conditions; peripheral pressure, a moist or lubricated surface of contact and possibly warmth being sufficient to elicit intromission. The ejaculatory reflex is normally elicited by the same stimuli as intromission but warmth, lubrication, pressure and friction appear to play some part in all animals although they are of relatively greater importance in some than in others. The ejaculatory reflex may also become conditioned to external stimuli. The whole pattern of sexual behaviour of the male will be determined by the presentation of appropriate stimuli, both conditioned and unconditioned in an appropriate sequence.

Much has been learned recently of the extent to which the basic reflexes can be conditioned by environmental stimuli as a result of the experience gained of maintaining bulls at centres for the collection of semen for artificial insemination. It is of great economic importance that these males should retain sexual potency and fertility. Yet it has been a common experience at many centres, that after a period of continuous use some bulls may show a gradual or even rapid decline in potency and fertility. The bull becomes slow to mount, the ejaculatory reflex weak and the volume of semen small. The spermatozoa produced in a weak ejaculation may have activity, longevity, and fertilizing capacity below normal. In many cases this change in behaviour may be traced to the gradual building up of conditioned inhibitions associated with slight deviations from the normal technique of collection. The artificial vagina may have been used repeatedly while too hot or too cold, the angle at which it was held may have given pain to the animal. Apart from correcting faults of technique and reducing the frequency of collections, every effort may have to be made to break the environmental associations which may have become conditioned inhibitors.

The work on bulls has been of considerable value within the species but although it might be considered premature to compare the results with those met by the human gynæcologist or sex psychiatrist in practice, there are many obvious parallels with human behaviour and the work may shed some light on human problems of impotence and sterility.

Dr. John Hammond said that the papers that afternoon had opened a very promising field for investigations on farm animals. A thorough study of animal behaviour would not only be useful to the veterinarians in making diagnoses—for they had a much more difficult job than the doctor, whose patient can tell him how he feels and what he

wants—but it also formed a scientific basis for what we knew as animal management. A good stockman by keen observation knew what an animal wanted and saw that it got it: studies such as Prof. Johnstone-Wallace had made showed promise of resolving this art of animal management into a science and so enabling great progress to be made in animal health and productivity. He hoped that more studies would be made on these lines, particularly in sheep which were dependent on grazing to an even greater extent than cattle.

Dr. E. S. Stern said that in regard to Dr. C. S. Myers's paper, the cuckoo laid her egg in the type of nest in which she was reared, and presumably, if the egg was laid in the nest of another variety of bird, a change of habit would occur in the offspring to this latter variety. He thought the definition of " Instinct", which Dr. Myers had modified from McDougall, was unsatisfactory, in that it postulated that the animals were able to *feel* about a particular matter, and it must be doubted whether we had any evidence of emotional response in the lowest forms of animal life that still show instinctive behaviour.

Referring to Dr. W. H. Thorpe's address, Dr. Stern said that "habituation" seemed to be only another aspect of fatigue, and "imprinting" was merely learning by rote.

Prof. Johnstone-Wallace had illuminated many interesting problems on grazing, and he wished to draw attention to selective grazing, which was so much more a serious matter in the case of the horse.

It was interesting to note that Dr. Arthur Walton was meeting problems in the bull which had their counterpart in man, where the psychiatrist had occasionally to advise an alteration in method as married life progressed, in order to prevent the onset of partial impotence.

Mr. M. R. A. Chance said that a major problem confronting those who study animal behaviour from the point of view of comparative psychology was how instinctive behaviour was related to learning processes. The understanding of instinctive behaviour was relevant not only to the study of individual behaviour, because of the occurrence of rigid behaviour patterns during the mating seasons of animals and birds, and during migratory movements, but also because it might be a determining factor in the evolution of certain species. D. M. S. Watson explained the emergence of many divergent forms of reptiles from an original Plesiosaur stock, on the assumption that genetically divergent behaviour patterns provide an initial differentiation of function, upon which selection was able to develop correspondingly divergent forms. This demonstrated the reverse relationship between form and function to that now presented by Dr. A. Walton. Amongst higher mammals, learning takes an increasingly greater part in determining the behaviour of individuals. Through these studies, therefore, it might be possible to assess the degree to which learning processes influenced the survival of species.

Section of the History of Medicine

President—Sir WALTER LANGDON-BROWN, M.D.

[*May 3, 1944*]

Some Chapters in Cambridge Medical History.—IV. The Early Nineteenth Century from Pennington to Paget[1]

By Sir WALTER LANGDON-BROWN, M.D.

IT has been unkindly and rather unfairly said of William Blake that he had a foot in two ages and a place in neither. This description could be more accurately applied to Sir Isaac Pennington, whom William Pitt appointed Regius Professor of Physic at Cambridge on the death of Russell Plumptre in 1793, and who occupied the Chair till his death in 1817. He was of the *Gold-headed cane* school, but was too late to enjoy its full splendours. On the other hand, he lived to see the birth of a new and more scientific approach to medicine without actually participating in it. Indeed, he was the antithesis of the holder of the Chair at the next turn of the century, for Clifford Allbutt had a foot in two ages and achieved a place in both. One thing they had in common—a remarkable natural dignity. Indeed Pennington is now chiefly remembered by the tinted engraving of him duly robed as a Doctor of Physic in Ackerman's *History of the University of Cambridge* as the most dignified exponent of that order. Yet his record was by no means without merit. He entered St. John's College in 1762 as a sizar, when to be one resembled a public school fag, but was promoted to a scholarship four years later. He was a Wrangler and became a Fellow of his college, holding many college offices, including that of Linacre Lecturer for fifty years in conjunction with his other appointments. He was also put in charge of the college observatory. Entering St. George's Hospital, he qualified in 1773 and in the same year was elected Professor of Chemistry after a spirited public contest, as was then the custom. In 1785 he became Physician to Addenbrooke's Hospital. But it is by no means certain that he ever gave a lecture during his forty-four years' tenure of two professorial chairs.

In 1800 came a change in the University. After thirty years of litigation, rivalling Jarndyce v. Jarndyce, Sir George Downing's will founding the college named after him together with professorships of Law and Medicine at last became operative. Unfortunately, as was inevitable, so much of the available funds were exhausted by legal expenses that the College was always crippled for money until it sold some of its land to the University for the building of new laboratories in 1896, which partially relieved the strain on its finances. Only partially, for the College buildings have never been completed, and in 1930 the Downing Professorship of Medicine had to be abolished for lack of funds, while that of Law apparently may follow when its present holder vacates it. This crippling was doubly unfortunate for the Statutes of the new College were drafted on modern, greatly improved lines, and its early failure was quoted by the reactionaries to point the moral that reform was "dangerous if not fatal", with some effect. Perhaps the greatest lustre ever conferred on Downing was by the brilliant F. W. Maitland, who held the Professorship of Law for nearly twenty years, and who illuminated every topic he touched. The first Downing Professor of Medicine was Busick Harwood, who was already Professor of Anatomy and afterwards knighted. Henry Ainslie, a Senior Wrangler and then Physician to St. Thomas's was a much stronger candidate, but Harwood's friends brought on the election unexpectedly! Harwood did not shed much lustre on the Chair, and he seems to have been an unpleasant character. As a surgeon in India, he had amassed considerable wealth in the palmy days of the old East India Company, and on return to Cambridge he proceeded to live extravagantly, his conversation, according to Gunning, being "profligate and licentious in the extreme", while his obscene stories sickened even his Rabelaisian friends. His relations with the Regius, Pennington, were at first amicable, and they used to play pianoforte duets together. They were also

[1] Chapter I, "John Caius and the Revival of Learning," *Proc. R. Soc. Med.*, 35, 61.
Chapter II, "Francis Glisson and the Insurgent Century," *Proc. R. Soc. Med.*, 36, 17.
Chapter III, "William Heberden and the Age of Reason," *Proc. R. Soc. Med.*, 37, 53.

both leading figures in the Cambridge Volunteers, formed in the days when Napoleonic invasion was feared. There, they were associated with Lord Palmerston, and Henry Martyn, the Evangelical missionary. How the saintly Martyn reacted to Harwood's conversational methods has not been revealed. A childish greeting between the Regius and Downing Professors took the form of "Good morning Sir B. U. Sick?" the reply being, "Sir, I? Sik? I was never better in my life". Ultimately Harwood quarrelled with Pennington and sent him a challenge, which was contemptuously declined. The Trinity undergraduate who brought the cartel immediately posted off to London to have the story published, for he saw the news value of a scandal between two learned professors. Another incident occurred when Mansel, Master of Trinity, unctuously remarked "I am a prelate of the Church, Heaven knows how unworthy". Harwood replied, as he fled from the room, "Heaven does know, and so do I". Stevens says that Harwood ingeniously arranged for a presentation of plate to be made to him, the subscription being limited to two guineas, and then himself sent anonymously a banknote for £50. In one respect he was economical, for it is reported that he frequently dined off the turbot dissected in the previous day's demonstration. Decidedly not a pleasant person, and though we must place to his credit his great interest in blood transfusion, as Winstanley says, "all that we know of Harwood suggests that he was a very third-rate scientist".

It should be stated that the Downing Professor was expected to deal with pharmacology and materia medica, and one may suspect that the example of Heberden stimulated Sir George's trustees to insert this proviso in the Statutes, though until Latham held the Chair from 1872 to 1892, not much was done in this direction, nor were the duties energetically performed. One of Harwood's successors gave his lectures to a class of two in his breakfast room, and they often found the professor in bed.

Harwood died in 1814, and left instructions that he should be buried in the chapel of the college that had adopted him. But that chapel is still unbuilt, and a slab of stone between the Master's Lodge and the Hall marks the vault in which he lies, still waiting for its erection.

Pennington lived three years longer, but published no contributions to medicine, although he was the first Regius Professor of Physic to deliver the Harveian Oration at the College of Physicians. He died unmarried, and was a generous benefactor to his own college and to the University.

In the year of Pennington's death, 1817, the dry bones began to stir appropriately enough, in the department of Anatomy with the appointment of William Clark of Trinity who had been a pupil of Abernethy at Bart's. On his travels in Italy he acquired some fine anatomical models in Bologna, to which he later added other collections to form an anatomical museum. Shipley regards him as "one of the founders of the School of Biology at Cambridge". There were three professors of the same name at that time. He, as an anatomist, was nicknamed "Bone" Clark to distinguish him from "Stone" Clark the mineralogist, and "Tone" Clarke, Professor of Music. Stone Clark's lectures aroused general interest in science, and he had an audience of over 200. Bone Clark strenuously advocated the establishment of two chairs, one of human, the other of comparative anatomy, which was done in 1866, just after he resigned his Chair. After again an open contest Alfred Newton, of whom I shall speak later, was elected to the Chair of Comparative Anatomy, while George Humphry became Professor of Human Anatomy.

Meanwhile reform in the medical curriculum was being quietly carried out by Pennington's successor, John Haviland, to whom inadequate justice was done until the publication of Sir Humphry Rolleston's history of the Cambridge Medical School in 1932. Haviland obtained a Fellowship at St. John's College and received his medical education at Edinburgh and Bart's; he was only 32 when appointed Regius. He was Harveian Orator in the year of Queen Victoria's accession. The requirements for the degree of M.B. had hitherto been ridiculously inadequate—the candidate had merely to reside for nine terms, retain his name on the books for five years, witness two dissections and keep a single Act. This could not go on safely, for the College of Physicians were petitioning for the right to confer degrees. "The Medical School was held indeed in justified contempt . . . It is significant that the eighteenth century champions of the University were generally content to give [it] no more than a passing mention" (Winstanley). Sir Humphry Rolleston justly said: "The Medical School of Cambridge owes much more to him than is now realized. For he was the first, beginning in 1819, to give regular courses of 50 lectures annually in pathology and the practice of medicine . . . and to make the medical examinations a real test. On February 27, 1829, entirely as the result of his insistence and influence, the Senate passed a Grace which recast the medical curriculum and examinations, thus laying the foundations of the present time.

As he wrote little, and personal memories die comparatively young, Haviland's name is seldom mentioned now, but if the progress of the Medical School since his time be a monument to his saving grace, he could hardly have wished for a greater."

Changes were occurring in other directions, which at first had an indirect but ultimately an important direct influence on the medical school. The full story has been told in the history of Trinity College by G. M. Trevelyan, the present Master. After the passing of the Reform Bill in 1832, it was expected that nonconformists would be admitted to the universities, but the House of Lords thought otherwise. Connop Thirlwall, Assistant Tutor of Trinity, wrote a pamphlet advocating the admission of nonconformists, and also the abolition of compulsory Chapels, which, he said, were impious and unprofitable to the religious life. When told that the alternative was between compulsory religion and no religion at all, he replied, "The difference is too subtle for my grasp". Christopher Wordsworth the younger brother and, in Trevelyan's words, a surly edition of the poet, was Master of the College at the time. His extreme toryism was unpalatable to the majority of the Fellows, so when he dismissed Thirlwall from his Assistant Tutorship for daring to express such opinions, even those who differed from Thirlwall, hotly resented his action. Not that Thirlwall suffered long, for he soon became Bishop of St. David's where he proved himself; according to Coulton, the most learned Bishop on the Bench, with the single exception of Stubbs of Oxford. He certainly proved the most enlightened. But Wordsworth deservedly found himself more than ever isolated in the College and would have retired had he not convinced himself that as long as a Whig government was in power, they would advise the Crown to appoint a Liberal, probably Adam Sedgwick the elder, who, as a scientist and an avowed reformer, was anathema to him. And so he clung to office until 1841 when a Conservative government came into office, whereupon, as Trevelyan phrases it, Wordsworth resigned with comic promptitude and Peel at once advised the Queen to appoint William Whewell, as he had hoped. But Whewell proved more of a reformer than Wordsworth anticipated, and a more effective one than the blustering Adam Sedgwick. Whewell was not primarily a scientist, as may be judged by his wish that a century should pass before new discoveries in science be admitted into courses of academical instruction. It is not surprising that this shook Sir Robert Peel's belief in Whewell as a reformer. This was the sort of thing which convinced Lord John Russell that the University could not be trusted to reform itself from within. Nevertheless, having read that part of Whewell's *Bridgewater Treatise* which deals with "the unique properties of water", I am amazed at his brilliant and prophetic insight into scientific problems, which he had elaborated in his *History of the Inductive Sciences* before he became Master. So Wordsworth had been warned! Sidney Smith's well-known epigram on Whewell that "science was his forte and omniscience his foible" carries an unfair imputation. It was he who induced the University against strong opposition to elect the Prince Consort as Chancellor because he knew him to be an educational reformer after his own heart, and also because he desired reform to take place from within and not to be imposed from without. The Prince with the aid of Whewell and Dr. Phillpott, Master of St. Catherine's, effected the introduction of the Natural Sciences Tripos in 1848. This was a great step forward as an encouragement to a more scientific preliminary training for medicine, and gradually increased the attractions of the Cambridge Medical School. Only gradually, because of the inadequate opportunities for practical work owing to very insufficient laboratories. Surprise has often been expressed at the long delay in establishing University laboratories, because it is forgotten that until the Statutes of 1882 the University was poor although the Colleges were rich. For centuries pious benefactions had been made to the latter, but seldom to the former. It was the close corporation of a man's college which excited his loyalty and affection. I believe that Trinity had previously offered to tax itself voluntarily in the interest of the University Chest if others would do the same, but only five colleges were willing. Now each is compulsorily taxed according to its means and all teaching has become more centralized. Previously, some colleges ran their own laboratories, and even in my time, St. John's, Caius, Sidney and Downing still had their own chemical ones, although the University laboratory was already in existence. The one in which I learned my chemistry has now been converted into much-needed baths, a luxury long postponed on the ground that the term lasted only eight weeks! Edward Bowen of Harrow fame regarded even an occasional hot bath as "later Roman". Cleanliness might be next to Godliness, *sed longo intervallo*!

When Haviland died in 1851, Macaulay happened to be at Windsor Castle, and the Prince Consort discussed the vacancy with him. The Prince was very doubtful whether one of the heads of the profession could be induced to fill it. His doubts were justified for the Crown appointed Henry Hayles Bond who could not be so described. He had

been clinical clerk at Bart's to the famous Peter Mere Latham and was one of the first in this country to use the stethoscope. His is preserved in Addenbrooke's. Rolleston said of him that he was "a man of sterling integrity, averse from personal advertisement . . . truly sincere, considerate and kindhearted". He induced the Senate to appoint an Assessor to assist in the judging of theses for the M.D. degree, an arrangement which in my turn I personally found a great help. But he was not otherwise an active reformer, and authority passed into the hands of George Paget long before he succeeded Bond on his resignation in 1872.

George Edward Paget was born in 1809, a vintage year for birth of talent and genius, and was thus five years older than his brother, James. These two brothers have been compared to another pair, William and John Hunter, physician and surgeon respectively; in each case the surgeon became the more famous. But unlike the Hunters, the Paget brothers remained close friends. Their family is rich in inherited talent, a remarkable record of professional attainments matched by high character. After Charterhouse, where Thackeray was his schoolfellow, Paget entered Caius College and became a Fellow there, holding many college offices. In 1842 during the Regius Professorship of Haviland, he initiated clinical examinations in the final M.B., the first to be held anywhere in the United Kingdom, but now universal. From 1851 until his promotion as Regius, he was Linacre Lecturer and he was Physician to Addenbrooke's for forty-five years. In his Harveian Oration of 1866 he prophesied the extension of vaccine therapy and immunology. From 1869 to 1874 he was President of the General Medical Council. His merits were further recognized by being elected F.R.S. and being made K.C.B. He was also President of the B.M.A. in 1864. His literary output, however, was small, chiefly on obscure nervous symptoms, and he evidently recognized what we now call catalepsy and other borderlands of epilepsy as well as the Plummer-Vinson Syndrome.

The old idea of an Act for a degree involved a disputation and Paget was apt to translate this literally. He liked to explain this when asked to approve the title for a thesis, saying that he had once been obliged to refuse the proposition "That mother's milk is the best for infants" as he was incapable of bringing arguments against it.

It lies outside my present topic to show what an important part he played in the Cambridge of his generation. His influence in establishing the Natural Sciences Tripos desired by the Prince Consort was considerable. One of his greatest services was, however, the part he played with his brother James, in bringing George Humphry from Bart's to Cambridge in 1842. Of the tremendous vitalizing force of Humphry I have spoken in a previous paper. Among other things, Humphry agitated for a Chair of Physiology. But there were difficulties and delays. Once again, as in Stephen Hales' time, Trinity College came to the rescue and established a Prelectorship in Physiology, carrying a Fellowship with it. On Huxley's recommendation, Michael Foster was brought from University College to hold that office in 1870. Thus the modern history of the Medical School began and was carried to triumphant success by the great triumvirate of Paget, Humphry and Foster. It was the psychological moment for this to be formed, for the ground had been prepared against many difficulties. Before briefly explaining the reason for these, it may be of interest to refer to two men who took office before 1870 but were still active in my own undergraduate days. They were striking personalities belonging to an age when untrammelled expression of peculiarities in a way which would hardly be acceptable to-day was by no means rare.

Alfred Newton was Professor of Zoology from 1866 to 1907 and he was mainly interested in birds. Dr. Lewis Shore told us he dutifully attended Newton's lectures when working for the first M.B., but as a whole term was devoted to one class of birds, he didn't benefit much. Shipley said that Newton's lectures were desperately dry and very formal; at times he was the sole auditor. Not that that made any difference to the Professor. He steadily and relentlessly read on—"the majority of you now present know" or "most of my audience are well aware", which left Shipley in considerable doubt as to what parts of him were "the majority" and which "the most". Yet his informal talks were most helpful.

Newton's Sunday evenings in Magdalene were great institutions for all who cared about biological science. He sat in an armchair just within the doors and invariably wore mittens. Sir Arthur Shipley's description of those evenings in his delightful *Cambridge Cameos* exactly accords with my own recollections. "The room was plainly but comfortably furnished in the mode of the Victorian period; the fire was very hot, the guests were seated in a large semicircle of chairs, something like Christy Minstrels of our boyish days . . . often there were awkward pauses but the Professor sat through them all, making spills out of old letters and smoking pipe after pipe. . . . These Sunday evenings were a little formal and a little dull; we were all a little afraid

of the Professor and much more afraid of ourselves. . . . And yet in spite of these obvious disadvantages [they] saved Zoology as the science of living animals in Cambridge." I am grateful to Newton for giving me the opportunity of meeting Alfred Russell Wallace at lunch. "As most of my audience are well aware", Wallace almost intuitively hit on the idea of Natural Selection at which Darwin had been working for twenty years. Darwin had been urged to publish an abstract of his work to prevent it being anticipated. And so it very nearly was, but the two men happened to find they had formed the same theory and so arranged to make their communication jointly to the Linnean Society. This is a pleasing variant on the disputes about priority which sometimes deface scientific literature. Newton was one of the first zoologists of repute to accept the theory, and it was a real satisfaction to meet and talk to Wallace in his rooms just thirty-five years after the publication of *The Origin of Species*. Although Newton was a die-hard in most things, he encouraged his juniors even when he was not interested in their ideas, for instance Frank Balfour's embryology and William Bateson's Mendelism.

The other man is John Willis Clark, son of "Bone" Clark, the Professor of Anatomy and of Mary Willis, whose father attended George III in his mental illness in 1810. Her brother, Professor Willis, was engaged on *The Architectural History of the University of Cambridge*, but this was in a very incomplete form when he died in 1875. So John Willis Clark his nephew, undertook the laborious task of revision and completion. The result duly appeared in three monumental volumes with an additional one of plans, past and present, of all the colleges, and the work comprises much besides architecture. It is the joy of every lover of Cambridge who is fortunate enough to possess a copy, and places them under a deep debt of gratitude to both Willis and Clark.

At the same time as the Chair of Zoology was established and filled by Newton, the Museum of Comparative Anatomy and Zoology was separated from that of Human Anatomy, and John Willis Clark was appointed Curator. He held that office from 1866 to 1891, when he became Registrar till his death in 1910. We knew him as J. W. but to his intimates he was simply J. For nearly sixty years he was a striking figure in the University with his picturesque hair and beard, both worn rather long. Out of kindness to Foster, he used to manage the Physiological Laboratory accounts and collect the fees; yet the undergraduates firmly believed he did this to collect the odd shillings out of the guineas as his commission. Though J. W. had a peppery temper and a considerable command of "language", he was kindhearted and hospitable, though, naturally, not universally popular.

This communication is intended to fill the gap between the ground covered by my paper on William Heberden and that on the rise of the Cambridge Medical School.[1] For in spite of serious deficiencies the early part of the nineteenth century was the seedtime of university reform, and it is of some interest to inquire why so much of the seed fell on stony ground, thus delaying the growth of the School. For there was a real desire for reform, the need for which the complacency of the eighteenth century had never felt. The University was still in the thrall of the Elizabethan Statutes which could not be changed in the smallest detail without the consent of the Crown although many were impossible of fulfilment and some frankly ridiculous under more modern conditions. Consequently, when inconvenient they were ignored, though there was always the danger of some precisian suddenly invoking them to suit his own purpose. Politically, we know the disadvantage of the survival of obsolete laws, yet little is done to cut out this dead wood. Is it surprising that the Universities were not quick to do so? I will try to put as fairly as I can, the case as the reactionaries saw it, while fundamentally disagreeing with them.

Oxford and Cambridge arose as religious but not monastic institutions. Indeed, at Cambridge the earlier colleges were founded largely to counter-balance the influence of the Friars who had already firmly established themselves there. Does not this suggest that thus early there was a dislike of foreign influences in English religious life, a dislike which culminated in the Reformation? Nevertheless, the monastic model was fairly closely followed. Since until the time of the Tudors the clergy were the only people with any pretension of or desire for learning, it was natural that the Universities should be devoted to their interests, and the pious benefactors of colleges wished to help in that direction. In itself, the ideal of an oasis of learning and religion amid all the disturbances of outside, was admirable. A self-contained community within college gates, a Master, Olympian but benevolent, Fellows set free from all other ties to devote themselves to learning, Tutors teaching and living actually in the same chambers as their pupils so as to supervise every detail of their lives, all dining together in Hall and worshipping together daily in the College chapel. Behind all this activity the University

[1] "W. H. Gaskell and the Cambridge Medical School". *Proc. R. Soc. Med.*, 1939, 33, 1.

was merely a shadowy background, ordering matriculation and the acts for graduation. That accomplished, there was to issue a steady stream of young men carrying sound learning and religion all over the countryside. College gates, however, cannot exclude human nature. "The high that proved too high, the heroic for earth too hard" was exemplified. Bottled up like this, turbulent youth and self-indulgent age proved an incompatible and often explosive mixture. Twice, at the Renaissance and during the insurgence of the seventeenth century, there was an inroad into this artificial world, but it settled down more complacently than ever into its groove during the eighteenth century. "Then the conscience of the Cambridge world had become atrophied. . . . The story for the most part is one of broken oaths, violated statutes and cynical disregard of testamentary wishes." In the medical school "events moved in a vicious circle. The Professors were indolent because the School was so insignificant, and the School was so insignificant because of the indolence of the Professors. . . . It was not until the nineteenth century, when the fierce light of public opinion began to beat upon Cambridge, that abuse only honoured by time was eradicated" (Winstanley).

Now that it was seriously challenged, we can hardly wonder if men who had grown up in the tradition, and believed the old ideal was yet capable of revival, passionately resented changes which they honestly believed would shatter it. We must remember that even as late as 1841 half the students were destined for the Church. Right into the nineteenth century all but a few Fellows had to take orders within a specified time and remain celibate. Thus all the biggest prizes were reserved to the clergy, and one need not be over-cynical to be struck by the coincidence that when this was no longer the case there was a sharp fall in the numbers reading for the Church.

The plight of Classics is surprising at a time when ability to read and write Latin easily was regarded as part of the equipment of any educated man. Yet there was no classical Tripos established until 1822. As I have criticized Christopher Wordsworth, I must place that reform to his credit. Previously it was maintained that the great prizes of Craven scholarships and Chancellor's medals were sufficient stimulus though clearly they only affected the most ambitious students. If this had been the attitude towards Classics, what hope was there for natural science?

The dice were heavily loaded against reform by the attitude of most of the Heads of Houses. In those days when a man by merit or intrigue became Master of a college, he was a man apart. He could marry, and enter into one of the most exclusive sets in existence. Socially the families belonging to the Masters' Lodges had little to do with the rest of the University; even Professors were regarded as below the salt! Academically, the effect of this attitude was disastrous. Therefore, the reformers started with an attack on the Heads of Houses, and after a struggle a popularly elected Council of the Senate replaced the autocracy. Indeed, Lord John Russell realized that there was a real intention to reform from within. Nevertheless, neither University could satisfy the external demands; Oxford being the more recalcitrant, received earlier and severer handling by the Statutory Commission, in 1854, but only a year later Cambridge had her turn. To-day in the retrospect, it would appear that even then some obvious evils were left unreformed. The reconstitution of a Heresy Board smacked of the Middle Ages, religious tests were still imposed and celibacy of Fellows with some exceptions enforced. Not until 1882 was this ban on marriage removed, and that year sixty brides arrived in Cambridge, inaugurating a new social area. Nor has their introduction had the disastrous effects anticipated.

The general effect of the 1855 Statutory Commission was to increase the authority of the University at the expense of the Colleges, a process continued in 1882, and carried to its logical conclusion in 1925 when Treasury Grants were made, not to colleges, but to the University. Teaching has now become almost entirely centralized, except for supervisors of studies in colleges, who have practically killed private tuition which certainly ought not to have been required.

This brief résumé of the gradual changes in the nineteenth century, will, I hope, serve to explain the slow development of the Medical School prior to 1870. Dr. Arnold Chaplin has shown that from 1500 to 1876, the average number graduating in medicine was only four, and the numbers only increased slowly after this until the 80's, although the candidates for the Natural Sciences Tripos became more numerous earlier. Yet it remains a surprising fact to me that although the University has been in existence for more than 700 years, its Medical School as a really going concern, is literally comprised within my own lifetime.

Section of Laryngology

President—W. M. MOLLISON, M.Ch.

[*May* 5, 1944]

DISCUSSION ON LYMPHOID DISEASES OF UPPER RESPIRATORY TRACT

A. H. T. Robb-Smith: There is a large amount of lymphoid tissue in the upper respiratory tract, and all of it is of the lympho-epithelial type; that is to say it has only efferent lymphatics and the mucous surface is covered by epithelium of a peculiar type, having no basement membrane, with the result that the two types of cell merge in the boundary zone. Apart from this, the morphology of the lymphoid portions is in no way different cytologically or anatomically from lymph nodes, being divisible into follicles, sinus and medulla with a variety of cell types of variable potencies. In connective tissues throughout the body, and this applies with equal force to the connective tissue of the upper respiratory tract, there are inconspicuous mesenchymal cells which have retained their embryonic potencies in the adult organism and may, under suitable stimuli, differentiate to form any type of cell within their potency so that new formed areas of lymphoid tissue may appear as the result of such stimuli. The disorders of the lymphoid tissue of any region of the body must be divided into two categories: (*a*) those initiated by local conditions limited to that region: (*b*) those in which there is a generalized abnormality of the lymphoid tissue throughout the body and, therefore, the lymphoid tissue of the special region undergoes a similar process. It may be from a clinical point of view, that the regional involvement is the presenting symptom of a generalized lymphoid disorder but that in no way justifies its isolation from the point of view of nosography. In either category the change in the lymphoid tissue may be reactive, that is to say the result of stimuli of which we have some knowledge, or idiopathic, in which we have at the present no real knowledge of ætiology, though we may know much about the morphogenesis of the condition.

The term *"reticulosis"* has become unduly popular as it sounds impressive even if its meaning is not understood. Reticulosis was coined some fourteen years ago as a generic morphological term in pathology to describe hyperplastic conditions of the reticular tissue, and embraces the leukæmias, Hodgkin's disease and kindred idiopathic conditions, and, from a reactive point of view, the morphological changes occurring in the tissues in tuberculosis and typhoid fever; reticulosarcoma is its neoplastic counterpart. It is comparable with other generic terms such as arthritis, neuritis, or catarrh though it is used more strictly in a morphological sense; to say that a patient has "a touch of reticulosis" means no more than to say that a patient has lymphoid hyperplasia. On the other hand when suitably qualified it indicates the particular type of hyperplasia, thus Hodgkin's disease or lymphadenoma verum may be described as fibromyeloid medullary reticulosis, or leukæmia as "myeloid or lymphoid medullary reticulosis", but the commonly used terms are preferable as they are shorter and, provided they are used strictly on the basis of good clinical or pathological criteria, just as acceptable to the systematist. However, a critical study of pathological conditions formerly grouped under the two headings of atypical Hodgkin's disease or pseudo-leukæmia has made possible the recognition of conditions with a definite natural history and morphology. As these have at present no clinical names it is necessary to use morphological descriptive terms based on histological criteria. These terms are cumbersome for the lack of a satisfactory shorthand such as chemists use. Thus we may have to say that a patient is suffering from lymphoid follicular reticulosis or lympho-reticular medullary reticulosis but such

was merely a shadowy background, ordering matriculation and the acts for graduation. That accomplished, there was to issue a steady stream of young men carrying sound learning and religion all over the countryside. College gates, however, cannot exclude human nature. "The high that proved too high, the heroic for earth too hard" was exemplified. Bottled up like this, turbulent youth and self-indulgent age proved an incompatible and often explosive mixture. Twice, at the Renaissance and during the insurgence of the seventeenth century, there was an inroad into this artificial world, but it settled down more complacently than ever into its groove during the eighteenth century. "Then the conscience of the Cambridge world had become atrophied. . . . The story for the most part is one of broken oaths, violated statutes and cynical disregard of testamentary wishes." In the medical school "events moved in a vicious circle. The Professors were indolent because the School was so insignificant, and the School was so insignificant because of the indolence of the Professors. . . . It was not until the nineteenth century, when the fierce light of public opinion began to beat upon Cambridge, that abuse only honoured by time was eradicated" (Winstanley).

Now that it was seriously challenged, we can hardly wonder if men who had grown up in the tradition, and believed the old ideal was yet capable of revival, passionately resented changes which they honestly believed would shatter it. We must remember that even as late as 1841 half the students were destined for the Church. Right into the nineteenth century all but a few Fellows had to take orders within a specified time and remain celibate. Thus all the biggest prizes were reserved to the clergy, and one need not be over-cynical to be struck by the coincidence that when this was no longer the case there was a sharp fall in the numbers reading for the Church.

The plight of Classics is surprising at a time when ability to read and write Latin easily was regarded as part of the equipment of any educated man. Yet there was no classical Tripos established until 1822. As I have criticized Christopher Wordsworth, I must place that reform to his credit. Previously it was maintained that the great prizes of Craven scholarships and Chancellor's medals were sufficient stimulus though clearly they only affected the most ambitious students. If this had been the attitude towards Classics, what hope was there for natural science?

The dice were heavily loaded against reform by the attitude of most of the Heads of Houses. In those days when a man by merit or intrigue became Master of a college, he was a man apart. He could marry, and enter into one of the most exclusive sets in existence. Socially the families belonging to the Masters' Lodges had little to do with the rest of the University; even Professors were regarded as below the salt! Academically, the effect of this attitude was disastrous. Therefore, the reformers started with an attack on the Heads of Houses, and after a struggle a popularly elected Council of the Senate replaced the autocracy. Indeed, Lord John Russell realized that there was a real intention to reform from within. Nevertheless, neither University could satisfy the external demands; Oxford being the more recalcitrant, received earlier and severer handling by the Statutory Commission, in 1854, but only a year later Cambridge had her turn. To-day in the retrospect, it would appear that even then some obvious evils were left unreformed. The reconstitution of a Heresy Board smacked of the Middle Ages, religious tests were still imposed and celibacy of Fellows with some exceptions enforced. Not until 1882 was this ban on marriage removed, and that year sixty brides arrived in Cambridge, inaugurating a new social area. Nor has their introduction had the disastrous effects anticipated.

The general effect of the 1855 *Statutory Commission* was to increase the authority of the University at the expense of the Colleges, a process continued in 1882, and carried to its logical conclusion in 1925 when Treasury Grants were made, not to colleges, but to the University. Teaching has now become almost entirely centralized, except for supervisors of studies in colleges, who have practically killed private tuition which certainly ought not to have been required.

This brief résumé of the gradual changes in the nineteenth century, will, I hope, serve to explain the slow development of the Medical School prior to 1870. Dr. Arnold Chaplin has shown that from 1500 to 1876, the average number graduating in medicine was only four, and the numbers only increased slowly after this until the 80's, although the candidates for the Natural Sciences Tripos became more numerous earlier. Yet it remains a surprising fact to me that although the University has been in existence for more than 700 years, its Medical School as a really going concern, is literally comprised within my own lifetime.

treatment is that appropriate to the causative factors, or whether it is part of a generalized lymphoid hyperplasia, even where the nasopharyngeal symptom is the primary manifestation; the treatment is then that of the general disease and a local eradication is no justification for assuming a cure.

V. E. Negus (*Chronic hyperplasia of the pharynx, 5 cases*): In 1901, Dr. A. Brown Kelly described a case of "Sclerotic Hyperplasia of the Pharynx and Nasopharynx" (*Lancet*, April 6, 1901).

The patient had nasal obstruction and suffered from choking fits. The uvula was enlarged, pale, fibrous, and firm; movable, firm prominent bands of greyish colour were present on either side of the posterior pharyngeal wall, passing up into the nasopharynx and down to the upper end of the œsophagus and overhanging the arytenoid regions. Sections from the uvula showed chronic hyperplasia of the interstitial tissues, with no tendency towards degeneration and with no appearance of any specific micro-organisms. The condition was unchanged 14 years later.

Sir Felix Semon described in 1902 "a case of obscure lardaceous-looking variable infiltration of the uvula, soft palate and right arytenoid cartilage in a lady aged 30". It was similar to Dr. Brown Kelly's description (*Proc. Laryng. Soc., Lond.*, 1902-3, 10, 11). The patient had occasional difficulty in swallowing. Semon also referred to other cases (*Lancet*, February 25, 1905); one showing involvement of the larynx, there being œdematous infiltration of the arytenoids.

A report on sections by Professor Shattock referred to the intact and normal state of the investing epithelium, the increase in size of the tissues being due to a diffuse formation of finely fibrillar connective tissue, in the central part of which there occurred small groups of fat cells. There were denser collections of cells bearing an obvious relation to the smaller blood-vessels, mainly at the periphery of the section. The cells consisted of lymphocytes and intermingled plasma cells: no mast cells or eosinophils were present in the section. There was a mesh of fine elastic fibrils pervading the connective tissue. Some capillaries a short way beneath the epithelium were plugged as a result of endothelial proliferation. No micro-organisms were demonstrated.

There were none of the structural features of tuberculosis, syphilis or rhinoscleroma nor of neuro-fibromatous pachyderma. A lymphangiomatous and lymphangiectatic lesion was excluded.

"The histological changes approach most nearly to those met with in hyperplastic rhinitis in its later, or what has been called its secondary stage."

Dr. A. Logan Turner described similar cases in 1914, one requiring tracheotomy; in one the bands on the lateral wall of the pharynx disappeared ten years from the date of first observation. Sections showed infiltration with small cells, mainly mononuclears. A further case was reported by Sir James Dundas-Grant (*Proc. Laryng. Soc., Lond.*, 1902-3, 10, 76).

In 1940 I saw a patient with Mr. Hope, the signs and symptoms corresponding to those mentioned above. Sections from our case were reported to show giant histiocytic sinus reticulosis or possibly sarcoidosis. Three other cases have been seen by me since that date and possibly a fourth, all similar as regards symptoms and clinical appearances; Case 4 has developed a somewhat inflammatory appearance since her first examination, but otherwise the condition has appeared indolent. There have been spontaneous local changes but treatment with deep X-ray therapy and with vitamins has had little obvious effect.

A fifth case, differing in appearance, is included as it was diagnosed microscopically as Boeck's sarcoidosis.

In his description of the reticuloses Robb-Smith includes in the follicular group a lymphoid and histiocytic type, to which it appears these cases may belong. He gives to this condition the title also of reactive follicular hyperplasia and germinal hyperplasia and describes the condition as occurring most commonly in lymph nodes draining sites of pyogenic infection. It would seem, therefore, that there may be an inflammatory cause for the hyperplasia, distinguishing it from other neoplastic conditions.

As the several cases described by Brown Kelly, Semon, Logan Turner and Dundas-Grant appear to be clinically similar to those seen by us, it is inferred that they have similar causation, whether it be Boeck's sarcoidosis or histiocytic reticulosis.

Their description under the heading of chronic hyperplasia of the pharynx and larynx is of course, too vague, as it gives no account of what elements are hyperplastic or for what reason.

The diagnosis of Boeck's sarcoidosis made by microscopical examination is not confirmed by clinical appearances or by radiography of the chest, except in Case 5, where there were shadows, possibly due to the disease.

ponderosities should mean something quite definite, both clinically and pathologically. However, the vast majority of locally limited processes are either reactive or neoplastic.

In the lymphoid hyperplasia that may occur in association with chronic inflammatory conditions of the nasopharynx the agent may be microbic; in other cases it is not so easy to identify any convincing causal organism and in these the character of the process may be somewhat bizarre but is essentially self-limiting.

I shall leave the neoplastic conditions as they do not truly come within the ambit of our discussion and consider those in which the nasopharyngeal lymphoid tissue has undergone hyperplasia as a result of a generalized process.

In the reactive group the most familiar example is measles, where a prodromal hyperplasia of a characteristic type affects lymphoid tissue throughout the body so that on occasions the pathologist examining a tonsil or appendix can tell the surgeon that the patient will develop measles before the rash has appeared; the same applies to a number of other infective diseases. Turning to the idiopathic group, the changes in leukæmia are illustrated by the firm nodular masses found in chronic lymphatic leukæmia and the swollen, often ulcerated, tonsils of acute leukæmia, often the first sign of the disease.

In the group without gross blood changes the nasopharyngeal tissue may be involved, I will recount two cases. A man aged about 50 complained of a rapid unilateral tonsillar enlargement and his doctor removed the tonsils; three years later enlarged glands appeared in the neck and a biopsy revealed one of the more benign types of primary lymphadenopathy —lymphoid follicular reticulosis. A section of the tonsils which had been kept in spirit showed the same changes as the lymphoid nodes. Although lymphoid follicular reticulosis is relatively benign it can and does cause death in a few years unless general radiotherapy is given. Another patient who had another type of lymphadenopathy, again relatively benign, but with a liability to appear in different sites at irregular intervals had been under observation for some years when he suddenly developed tonsillar enlargement. On removal, their histology was identical with the axillary nodes removed some four years previously. The case of Hodgkin's disease which is being shown to-day is of particular interest for it is my experience that involvement of the nasopharynx in this disease is rare and a survival for ten years in a case of true Hodgkin's disease is also uncommon. In a large series of cases 50% were dead in eighteen months irrespective of treatment and only 5% survived three years. In this case the original lymph node biopsy was not available but the diagnosis had been made by an experienced pathologist; the morphology of the laryngeal biopsy was such that although one would not make a positive diagnosis of Hodgkin's disease yet the appearances were in keeping with such a diagnosis.

I should like to say something of sarcoidosis of which two examples are being shown. The history of the condition is a perfect example of the dangers of over-specialization. At the latter part of the last century Jonathan Hutchinson described some curious cases of skin lesions sometimes associated with swollen fingers, which he named Mabey's malady after the first patient who suffered therefrom—a form of eponym all too seldom used. Subsequently Boeck and others described a group of skin lesions variously known as Boeck's sarcoid or lupus pernio.

Pathologists recognized a curious change in lymphoid nodes known as hyperplastic or endothelial tuberculosis in which there was no tendency to caseation and in which acid-fast bacilli would not be found. Then at the beginning of this century some other syndromes were recognized, ophthalmologists described a curious association of iridocyclitis with parotitis—Heerfordt's syndrome, and radiologists a cystic change in the fingers— osteitis multiplex cystica or Jungling's disease, and physicians the condition of chronic or benign miliary tuberculosis. It was not until 1914 that Schaumann suggested that these were all facets of the same disease, but partly because the war ensued and partly because he was misguided enough to suggest that the conditions should be called after himself or lymphogranuloma benigna, little attention was paid to his observations and it was not until about 1930, as the result of the writing of Pautrier and Longcope, that the unity of sarcoidosis was recognized. It is a curious malady essentially benign, protean in its manifestations, uniform in its histology which resembles the tuberculous granuloma in many respects. It has other bizarre affinities with tuberculosis for many of the lesions resemble those seen in lupus save that it does not cause the ulceration and scarring though it may be extremely disfiguring. In contrast to lupus the Mantoux reaction is negative and there are other features which enable a definite diagnosis and prognosis to be made. Its nature is in dispute, but my own feeling is that it is an unusual reaction to acid-fast bacilli of low virulence.

In conclusion I want to re-emphasize that in a lymphoid hyperplasia of the nasopharynx it is necessary to determine whether it is a local reactive condition in which the

are some reticulin fibrils running between them and the giant cell forms are very variable, some being large and more suggestive of foreign-body type. There is no doubly refractile material and I have not been able to demonstrate any acid-fast bacilli. . . . this case is more suggestive of a miliary lupoid than anything else, and the history would to some extent support that." A. H. T. Robb-Smith.

(4) A. L., female aged 56, complained of difficulty in swallowing for five weeks when first seen on 4.2.44; there was hoarseness at the onset. Relatives said the disability had been present for eighteen months. The dysphagia has now improved slightly.

The appearances, which have changed little, were of two smooth, pale columns on each side of the posterior pharyngeal wall, separated by a deep groove, extending up into the nasopharynx and down to overhang the aryepiglottic folds; the latter were much enlarged, especially the left. The epiglottis and vocal cords were unaffected.

There was no glossitis, no infection in the nose, sinuses or tonsils.

Direct examination showed obstruction of the mouth of the œsophagus by smooth surfaced infiltration.

It was thought that there might be malignant changes, even though no ulceration was present, but biopsy revealed chronic inflammatory infiltration only.

A biopsy from the left pharyngeal column showed the epidermis to be intact and natural in appearance, according to a report by Dr. Lloyd.

"Beneath, there is a moderate amount of lymphoid tissue showing germinal centres. These show some evidence of reactive hyperplasia and contain, in addition to lymphocytes, many reticulum cells.

The remainder of the subepithelial tissue shows evidence of chronic inflammation and fibrosis with no specific features. The fibrosis is fairly marked and does not appear to be of very long-standing, as the collagen fibrils are still delicate and the fibrocytes have plump, often cuneiform nuclei. There is slight dilatation of many lymphatics and in their neighbourhood and in that of the capillaries (which are only slightly congested) there is a chronic inflammatory cellular infiltration in which plasma cells are prominent.

Conclusion: Subepithelial chronic inflammatory hyperplasia with fibrosis."

Blood-count showed no anæmia or leucopenia: of 7,600 white cells, there were polys. 59%, lymphos. 30%, eosinos. 2%, monos. 9%.

The patient has been treated with vitamins A. B, C and D, and there is slight improvement in swallowing, but some increase of inflammatory appearances in the previously pale aryepiglottic folds.

(5) Male aged 25. *Boeck's sarcoid affecting palate and epiglottis.*—While in hospital for conjunctivitis, infiltration of the palate was noticed on examination; no symptoms were present. One brother had suffered from pulmonary tuberculosis, but the patient had no previous medical history of note.

Raised nodules were present on the hard palate and similar deposits on the free margin of the epiglottis. The latter appeared shrunken and the laryngeal border showed slight ulceration. There were no similar deposits in the nose, and the condition had not the typical appearance of lupus.

Wassermann test negative. Mantoux 1/10,000 negative. 1/1,000 positive.

Blood-count: Hb. 92%; C.I. 0·95%; R.B.C. 4,800,000; W.B.C. 7,200; polys. 58·0%; lymphos. 32·0%; monos. 6·0%; eosinos. 2·4%: basos. 1·6%.

Blood serum: Calcium 9·5 mg./100 c.c.; phosphorus 4·4 mg.; phosphatase 12·5 units; proteins 7 g.; albumin 4·6 g.; globulin 2·4 g.

X-ray examination: Apical scars are present in both lungs. Increased shadowing in right upper and mid zones.

Report on section: Boeck's sarcoid. Sections show some hypertrophy and slight chronic inflammation without ulceration of the overlying squamous epithelium. The dermis is infiltrated by a number of discrete, well-defined miliary lupoid nodules, consisting of a collection of epithelioid cells and giant cells of the Langhans' type, with some lymphocytes. Some of the giant cells show hæmatoxyphil bodies in their cytoplasm. These granulomata differ from tuberculous nodules in certain particulars: they are not confluent: there is very little central necrosis and no caseation. There is little inflammation around them, and there seems to be quiet collagen formation in relation to their edges; there is no ulceration and a Ziehl-Neelsen stain shows no tubercle bacilli.

Lt.-Col. Norton Canfield, U.S.A.M.C. (*Laryngeal obstruction probably due to Hodgkin's Disease*): R. R., a 28-year-old soldier, was first seen April 3, 1943, with a chief complaint of hoarseness. The present illness had existed for two months following a mild upper respiratory infection of which the hoarseness was thought to be a complication.

A report of the five cases is appended, but it is to be noted that Case 5 is included merely for comparison, as there were considerable clinical differences from the remainder and also from those described by Brown Kelly, Semon, Logan Turner and Dundas-Grant.

(1) E. G., female aged 55.

16.1.40: Sore throat and dysphagia one month with some obstruction of breathing. Tonsils removed in 1913. Patient is diabetic. Swelling of uvula and soft palate without ulceration; considerable œdematous swelling of the epiglottis, left aryepiglottic fold and slightly less on right side, with no involvement of cords. Left tonsillar region: enlarged and œdematous mass, firm and smooth. No evidence of pulmonary tuberculosis or of other changes in the lung fields. Wassermann negative. There was no rhinitis and no infection in the nasopharynx.

Biopsy 9.8.40: "The tonsil is covered by well formed squamous epithelium and the crypts are small. Scattered through the lymphoid tissue are small collections of endothelial cells mostly very clearly demarcated. In some of these areas are giant cells with numerous nuclei. Many plasma cells can be seen throughout the tonsil. While it is possible that the condition is an atypical tuberculosis, no tubercle bacilli could be found, there is no caseation, the arrangement of the endothelial cells and giant cells is not of the usual tuberculous type, and the giant cells are not typical tuberculous giant cells; the foci of endothelial cells appear to be for the most part coincident with the sinuses. These appearances suggest that the condition may be a giant cell histiocytic sinus reticulosis or possibly a sarcoidosis." Dr. Robb-Smith considered the condition to be comparable to those described as lympho-histiocytic reticulosis.

She was given deep X-ray therapy at the Middlesex Hospital, but with little change in the laryngeal condition, although the hyperplasia in the pharynx almost disappeared. Last seen in February 1944 with infiltration in the epilaryngeal region.

She also had treatment with ascorbic acid 50 mg. t.d.s.

(2) A. B., male aged 11.

23.7.40: He suffered from stridor at night, but nothing else. Bigger than his age physically but younger mentally. A previous report was that there was a hæmangio-endothelioma of low malignancy on the left side of the epiglottis.

Direct examination showed diffuse hypertrophy of the epiglottis and aryepiglottic folds, smooth, pale and more marked on the right side, where there were one or two protuberances; there was no ulceration. The vocal cords were overhung by the aryepiglottic folds but otherwise unaffected.

X-rays and blood examination showed no abnormal changes and nothing suggestive of pituitary abnormality.

Sections were previously reported as showing a lymphangioma with some obstruction or a granuloma with development of lymphatics.

Dr. Lloyd reports: "The section shows laryngeal epidermis and the tissues beneath. The epidermis is natural, except where it has been rubbed off. In the tissue beneath, the lymphatics are dilated and contain lymph and lymphocytes. Two or three of those shown in the section also contain aggregates of histiocytes mixed with lympho-cytes. There are small and larger foci of chronic inflammatory cellular infiltration, consisting chiefly of lymphocytes but also of plasma cells, among which can be seen multinucleate forms. These aggregates are often related in their position to the abnormal lymphatics, sometimes to blood-vessels. There is no obvious increase of collagen, and no fibroblastic activity. The appearances are those of a chronic inflammation of no specific kind, and do not suggest neoplasia."

(3) D. M., male aged 23.

In January 1942 this patient was under the care of Mr. Oxley, suffering from dyspnœa, so marked that sleep was interrupted; the cause was mainly enlargement of the soft palate and uvula, and, to a lesser degree, infiltration of the epiglottis and aryepiglottic folds. There was also pale swelling of the posterior pharyngeal walls on either side.

The former condition improved spontaneously and the latter was relieved to a certain extent by deep X-ray therapy. In October 1942 the symptoms of laryngeal obstruction became worse after a cold; there was some difficulty in swallowing and signs of Eustachian obstruction.

There was no obvious infection of nose, sinuses or teeth. Treatment with ascorbic acid and other vitamins was given, although tests showed no deficiency.

The pathological report on tissue from the pharynx was in favour of Boeck's sarcoidosis: "I am by no means satisfied that the condition is one of tuberculosis. The epithelium is comparatively intact and in the connective tissue there are circumscribed small epithelioid granulomata, none of which are confluent or show caseation. There

F. C. W. Capps (*Herniation of pharyngeal wall*, 2 cases): Male aged 20, first seen in June 1942. The history was a swelling first noticed under angle of jaw on right side. when aged 6. When aged 10 was "kicked" and swelling became more prominent. For three years it had been increasing in size. It did not cause any real disability. On examination in June 1942, a swelling over 2 in. in diameter could be produced below right angle of jaw on swallowing or could be inflated by patient. There was no definite outline, no fluctuation, no regurgitation into pharynx on pressure, and nothing could be seen on indirect examination of larynx and hypopharynx. X-rays with opaque swallow showed no definite pouch or outline. Opinions are sought as to whether any operative procedure should be adopted. Since first seen it has further increased in size.

Male aged 55. He first noticed swelling which appeared low down on right side of neck on coughing. Four months later both sides swelled. On coughing or inflating the pharynx a swelling appeared under and lateral to lower third of right sternomastoid and under the lower third of the left. These were resonant and coughing was caused on forcible collapse. Barium swallow showed no abnormality. The condition seems more likely to relate to the lung than to the pharyngeal wall.

The President said that he did not think either of these cases was herniation of the pharyngeal wall. He thought the first case a lymphangioma of the floor of the mouth, and the second, herniation of the apex of the lung.

J. C. Hogg suggested with regard to the first case that a needle exploration should be made.

Brigadier M. L. Formby said that he saw a similar case in 1929. The diagnosis then was aerocele, the swelling was tympanitic but the entrance into the pharynx or larynx could not be discovered. The swelling in the first case seemed dull on percussion.

C. A. Hutchinson said that it was not uncommon to see a similar appearance to that shown in the second case among young Scotsmen learning to play the pipes. Their lower necks became distended to a considerable degree while playing, and the condition was certainly of apical pulmonary origin, not pharyngeal. The condition was quite harmless.

T. Ritchie Rodger (*Section of tracheal tumour*): The symptoms in this case were dyspnœa, stridor, and hoarseness. Indirect laryngoscopy showed a tumour as large as a gooseberry just below the cords, its upper edge preventing complete approximation on phonation. The appearance was suggestive of fibroma. On March 23, 1944, operation by extended laryngofissure was carried out. The tumour was stripped off the mucoperichondrium of the posterior wall of the trachea, leaving a smooth surface without any suggestion of infiltration.

Pathological report by Professor M. J. Stewart, Leeds University to Dr. W. J. Purdy, of Beverley: "I concur in your view that this is a malignant tumour, but I think that it is at least in part of epidermoid type and the calcification is taking place in partially kerati- nized material rather than in secretion. Some of the spaces may be glandular lumina but there is a great deal of solid epithelium of distinctly epidermoid type. I form the impression that it is not very highly malignant, but it is a carcinoma."

Mr. Ritchie Rodger mentioned a companion case which Mr. J. H. Cobb of Sheffield had asked him to show. In clinical appearance it was almost identical with his own case. The operation in both cases was by extended laryngofissure. Mr. Cobb had sent the specimen and radiograph with his notes: "Case first seen on October 29, 1942. For more than twelve months had been troubled with dyspnœa on exertion and 'weakness' of voice. Examination of the larynx showed the vocal cords to be normal and fully mobile. Below the left cord was a smooth rounded tumour which encroached on the subglottic space. It was pale and suggested the appearance of a chondroma. The X-rays (tomo- graph) showed a tumour which occupied more than two-thirds of the subglottic region; there was no sign of infiltration of the thyroid cartilage. On November 27, 1942, laryngo- fissure was performed and the tumour was removed complete and without difficulty.

Pathologist's report (Dr. Hermitte): The section shows the structure of a myxo-

Past history.—Not significant except for one attack of axillary glandular swelling twelve years before which was diagnosed Hodgkin's disease and treated by X-radiation. Cure was considered satisfactory enough to be no deterrent for army induction. Otherwise the soldier had been healthy.

On examination.—A spare cachectic male adult with marked dysphonia and a wheezing respiration. There was telangiectasis in right axilla at the site of previous X-ray therapy. There was a small herpetic ulcer on the left anterior tonsillar pillar. The larynx was markedly obstructed by a proliferating granulomatous mass on both vocal cords and extending into the vestibule and the subglottic region. The mucosa was ulcerated on the right side. The airway was constricted by the mass to about one-fourth of its normal size. The larynx was easily cocainized and biopsy was taken by the indirect method. Microscopic examination revealed a process involving the lymphoid tissue and was named Hodgkin's disease by some pathologists. Those of our army hospital and Dr. A. H. T. Robb-Smith agreed on this diagnosis, but others, including the pathologist of the Middlesex Hospital and the Surgeon General's Office in the U.S.A. did not.

By the kind co-operation of Professor Windeyer at the Middlesex Hospital, X-radiation was administered. It was necessary to perform a tracheotomy which the patient tolerated well.

April 29: After 200 r units of radiation the larynx was much better. The airway had opened. Gradually the larynx returned to its normal condition. The voice improved and by June 20 there was no more evidence of the laryngeal lesion. Total tumour dose 2,490 r.

The patient's general condition improved at first, but later deteriorated. Ulcerations of the skin appeared and were considered manifestations of Hodgkin's disease. He was returned to the U.S.A. June 15, and word from our Surgeon General was that he was discharged to our Veterans' Administration in poor health about July 15. A microscopic section of the larynx is presented, and probably represents the type of case referred to by Mr. Victor Negus as reticulosis.

Ian G. Robin (*Three cases of frontal sinusitis*): These three ordinary cases demonstrate the still unsatisfactory treatment in most hands of chronic frontal sinusitis.

The first two patients had been operated on previously at other hospitals but in the third case he thought he had done a complete primary operation, and was much chastened to find cells full of chronic granulations at a second operation.

The first patient had had several operations on the right side, both external and internal. For the last year headaches had been diagnosed as functional. There was periodic swelling of eyebrow. Operation showed thick granulation tissue in three small recesses far back over orbit. There was also a small extradural abscess with about 1 c.c. of pus. Complete obliteration of whole sinus was performed and a tube left in the fronto-nasal duct for seven days. There had been complete relief of headaches for over twelve months.

The second case was one of bilateral frontal sinusitis secondary to long-standing pansinusitis. There had been multiple operations at various hospitals. Severe headaches were diagnosed on occasion as functional. X-rays demonstrated frontal sinus cells above orbit. Operation on right side three months ago showed pus under pressure in small extradural abscess above orbit, and two cells just anterior to optic foramen full of thickened granulations. Complete relief of headaches on right side followed operation.

In the third case there was persistent right frontal sinusitis following bilateral Caldwell-Luc operation and bifrontal ethmoidal operation in January 1943, for long-standing pansinusitis. At recent exploration of right frontal sinus three cells were found, far back over the right orbit, full of chronic granulations.

Operations on the first two cases are contemplated to fill in the eyebrow depressions, with pieces of iliac crest bone.

Lt.-Col. Norton Canfield said that these cases were also of interest to neurosurgeons. Recently he had been told by Col. R. G. Spurling, Neurosurgical Consultant, U.S.A.M.C., who had had considerable experience in these severe sinus cases, that a different sort of operative technique was being evolved; one which required a large incision and a tantalum implant to fill the skull defect. It seemed that they could take away as much bone as they wished, and that the cosmetic result afterwards, if not satisfactory to the patient, could be repaired by the use of tantalum.

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

[*May* 19, 1944]

The Metabolism and Therapeutic Use of Progesterone

By E. F. SCOWEN, F.R.C.P.

TEN years have now elapsed since the isolation of progesterone. Born, the embryologist, was the first to conceive the idea of the function of the corpus luteum. He postulated that the corpus luteum had an important function in pregnancy, since it occurred only in mammals and reached maximum development only during pregnancy. He did not live to prove his hypothesis, but Ludwig Fraenkel, in 1903, showed that removal of the corpora lutea in the first few days of pregnancy in the rabbit caused the embryos to disappear. He was unable to determine what happened to the embryos and it was not until 1928 that Corner showed that they survived and reached the uterus on the fourth day. There they shrivelled and disappeared because the endometrium had not been prepared for their arrival by the corpus luteum hormone.

Fraenkel's work was followed in 1907 by the discovery by Leo Loeb that the corpus luteum specifically alters the uterus of the guinea-pig so that implantation of the embryo becomes possible. In the guinea-pig no histological difference following the action of the corpus luteum is demonstrable but mechanical injury of the endometrium or the presence of the embryo results in the production of a deciduoma. Thus he found that in the guinea-pig deciduomata could only be produced during the luteal phase of the cycle and that removal of the corpus luteum prevented their formation.

In 1910 Bouin and Ancel began experiments which in the light of the present knowledge proved to be the most significant of all. They found that in rabbits in which ovulation had been induced by sterile mating, the uterus underwent very marked changes as the corpora lutea developed. It became congested and its epithelium grew rapidly, producing a very elaborate endometrium which was interpreted as being necessary for implantation. This change, later designated by Corner as progestation proliferation, did not occur if the corpora were removed. These classical observations established the corpus luteum as an endocrine gland, the function of which was to prepare the uterus for implantation of the embryo. These discoveries were rapidly followed by attempts to isolate the active substance, and in 1915 Herrmann proved that lipoid extraction of the corpus luteum and of the placenta contained an active substance which induced growth and congestion of the uterus and in some instances progestational proliferation of the endometrium. He, however, did not fully distinguish between the growth of the uterus and the change of the endometrium.

These experiments, with their faulty interpretation, delayed further knowledge until years later when it became apparent that the œstrogenic hormone was responsible for the

OCT.—OBSTET. 1

chondroma which at one part shows definite ossification. It appears benign, but myxomatous change in tumours is frequently suspicious. On the one hand ossification is probably a good sign.

Dyspnœa disappeared immediately after the operation and the voice became strong and normal after a few weeks. She has remained well."

C. A. Hutchinson (*Primary malignant subglottic tumour of trachea*): Subepithelial, no surface ulceration, involving the anterior and anterolateral aspects, and extending some 1 in. downwards. No evidence of any primary growth in any other organ.

Death occurred from bilateral lower lobar pneumonia of hypostatic, or rather pneumo-static, nature some six months after the patient—a woman aged 22 years—first reported sick with remittent attacks of dyspnœa.

Sections of the tumour show it to be a basal-cell carcinoma with pseudocystic changes. It does not originate from the thyroid gland, and probably arose from either: (*a*) ectopic thyroid tissue; (*b*) an ectopic salivary gland rest (vide Ewing, Neoplastic Diseases, 4th Ed., pages 788-9).

Specimens.—Larynx and trachea. Section of tumour. Shown by courtesy of Dr. L. H. D. Thornton, Salisbury.

Lt.-Col. Norton Canfield asked whether the tumour was visible by tracheoscopy. Could it be seen below the vocal cord?

C. A. Hutchinson said that he had never seen the patient himself; but understood that the tumour had been seen in the lumen of the trachea by another laryngologist on endoscopy, and that he had reported on it as presenting the appearance of a largish area of congestion in the subglottic area.

The question was how such a tumour could be diagnosed in the early stages, and when it was diagnosed what could be done for the case.

Section of Obstetrics and Gynæcology

President—MALCOLM DONALDSON, F.R.C.S., F.R.C.O.G.

[May 19, 1944]

The Metabolism and Therapeutic Use of Progesterone

By E. F. SCOWEN, F.R.C.P.

TEN years have now elapsed since the isolation of progesterone. Born, the embryo-logist, was the first to conceive the idea of the function of the corpus luteum. He postulated that the corpus luteum had an important function in pregnancy, since it occurred only in mammals and reached maximum development only during pregnancy. He did not live to prove his hypothesis, but Ludwig Fraenkel, in 1903, showed that removal of the corpora lutea in the first few days of pregnancy in the rabbit caused the embryos to disappear. He was unable to determine what happened to the embryos and it was not until 1928 that Corner showed that they survived and reached the uterus on the fourth day. There they shrivelled and disappeared because the endometrium had not been prepared for their arrival by the corpus luteum hormone.

Fraenkel's work was followed in 1907 by the discovery by Leo Loeb that the corpus luteum specifically alters the uterus of the guinea-pig so that implantation of the embryo becomes possible. In the guinea-pig no histological difference following the action of the corpus luteum is demonstrable but mechanical injury of the endometrium or the presence of the embryo results in the production of a deciduoma. Thus he found that in the guinea-pig deciduomata could only be produced during the luteal phase of the cycle and that removal of the corpus luteum prevented their formation.

In 1910 Bouin and Ancel began experiments which in the light of the present knowledge proved to be the most significant of all. They found that in rabbits in which ovulation had been induced by sterile mating, the uterus underwent very marked changes as the corpora lutea developed. It became congested and its epithelium grew rapidly, producing a very elaborate endometrium which was interpreted as being necessary for implantation. This change, later designated by Corner as progestation proliferation, did not occur if the corpora were removed. These classical observations established the corpus luteum as an endocrine gland, the function of which was to prepare the uterus for implantation of the embryo. These discoveries were rapidly followed by attempts to isolate the active substance, and in 1915 Herrmann proved that lipoid extraction of the corpus luteum and of the placenta contained an active substance which induced growth and congestion of the uterus and in some instances progestational proliferation of the endometrium. He, however, did not fully distinguish between the growth of the uterus and the change of the endometrium.

These experiments, with their faulty interpretation, delayed further knowledge until years later when it became apparent that the œstrogenic hormone was responsible for the

growth changes in the uterus and the action of the corpus luteum hormone was specific on the endometrium.

In 1928, Corner repeated the earlier work and found that extracts of the placenta would usually produce uterine growth, whereas extracts of the corpus luteum would only produce progestational proliferation of the endometrium. It was also discovered that the action of the corpus luteum hormone did not appear to be regular. Analysis of results showed that this irregularity was due to the test animal. Regular results could always be produced if sexually mature castrated animals were used, and the result was not seen in immature females.

This observation had two very important results. In the first place a method of bio-assay was possible, a fact of outstanding importance, as by its means was made possible the isolation later of the pure secretion progesterone. Secondly it led to the discovery that the corpus luteum hormone could only exert its action on a uterus previously sensitized by œstrogenic substance, and this was later demonstrated conclusively in animal experimentation and led to another method of bio-assay, the Clauberg method.

Many workers then proceeded with the search for the active substance, and in 1931 and 1932 crystalline substances were isolated with all the known activities of the corpus luteum. The methods, however, were long and tedious and the yields poor. It is doubtful whether in actual fact these earlier products were the pure substance, and the demonstration of pure progesterone was really made in 1934.

Two compounds were isolated which were apparently identical but found to have different melting points. They both had the same degree of activity and were shown to be different crystalline forms of the same substance and depended on the method of crystallization. These are spoken of as alpha and beta progesterone, and although it is still said sometimes that one is more potent than the other, there is no evidence on which this can be based. Following its isolation its chemical structure was proved almost simultaneously by Butenandt and by Fernholz and the hormone synthesized, the synthetic product being identical in all respects with the natural product. Additional proof was also found by another method. Marrian in 1929 whilst working on the œstrins in urine in women discovered an inactive alcoholic substance in the urine of pregnant women. This substance was found by Butenandt in 1930 to be pregnanediol. The close similarity of this structure to progesterone led to the surmise that this substance might be an excretion product of progesterone, particularly in view of the fact that Marrian only found this substance in pregancy urine. Butenandt also showed that this pregnanediol could be converted by chemical means back to progesterone. Following the discovery of the structure of progesterone and of pregnanediol, large numbers of allied substances were prepared, yet there remained only one which could produce the effects of the corpus luteum, namely progesterone. It appears to be a remarkably specific hormone.

The name progesterone has generally been adopted for the pure substance, and one international unit of progesterone is defined as the specific progestational activity of 1 mg. of the international standard preparation of beta progesterone, and 1 Corner-Allen unit is approximately equal to 1 mg. of either alpha or beta progesterone.

In 1936 Venning and Browne demonstrated that pregnanediol was not excreted as such in the urine but as a glucuronide, and that the complex sodium pregnanediol glucuronide could be extracted quantitatively from urine. Following this work it was discovered that this compound was present in the urine of women during the luteal phase of the cycle and during pregnancy, and was absent at all other times. The quantity excreted is considerable. In pregnancy there is a gradual increase in amount from the third month until the eighth month when between 70 and 80 mg. is excreted in twenty-four hours. It disappears within twenty-four hours of delivery. During the progestational phase of the menstrual cycle pregnanediol is excreted in variable amounts. There appears to be a wide range of normality, from 3 to 60 mg. These discoveries led to strong presumptive evidence that this compound was the excretory product of progesterone and final proof was found in that progesterone administered artificially could be recovered in a reasonable yield as pregnanediol glucuronide from the urine. It is stated that conversion is immediate and maximal during the luteal phase of the cycle or early pregnancy. These conditions are not, however, necessary, for I have shown that the conversion of injected progesterone will occur at any time in the cycle, that it will occur in the absence of the uterus and in the absence of the ovaries, and moreover, as we shall see later in some pathological conditions, there appears to be facilitation of this conversion after a passage of time. In addition the administration progesterone to healthy men is followed by the excretion of pregnanediol. I have

also shown that this conversion will also occur in castrate men. This method of excretion is peculiar to human beings. It does not occur even in monkeys, and moreover even after the injection of 1 g. of progesterone into the pregnant monkey there is no pregnanediol demonstrable in the urine.

From the results published elsewhere and from our own results it would appear that approximately half of the progesterone elaborated by the corpus luteum or given by injection appears in the urine as this complex. It is possible that more appears in an altered form.

Applying this knowledge to disease we began to investigate the condition metropathia hæmorrhagica. Investigations of untreated patients with this condition over the course of many months showed complete absence of the excretion of pregnanediol. We therefore considered that it might be possible in such patients to establish an artificial cycle of menstruation by substitution therapy with progesterone. To begin with we began by administering four doses given on alternate days of 20 mg. of progesterone. Following such therapy, usually on the second to fourth day, bleeding began from the uterus, or intensification of previous hæmorrhage. This bleeding lasted from four to seven days and then spontaneously ceased. If no further treatment was administered after a variable interval of amenorrhœa the condition usually relapsed, though in a few instances regular menstruation occurred from one to three periods. So frequent, however, was complete relapse that we decided to continue the treatment, designing the injections to produce as nearly as possible a regular cycle, but gradually diminishing the dose of progesterone. In this way it has proved possible to keep such patients well for periods up to seven years, which is our longest period of observation, and the dose required at the end of such time is as a rule 5 to 10 mg. each month. At the end of each six regular bleedings we stop treatment to see whether the patient will continue normally without further treatment and in a number this proves to be the case. In others, however, the condition relapses, usually after two to three months amenorrhœa. In some we have been fortunate in that they have become pregnant, the pregnancy has been normal and the disease has not reappeared after the pregnancy.

We have investigated the behaviour of such patients to progesterone and we have followed the metabolism of progesterone in such patients. We were surprised to discover that following the total dose of 80 mg. of progesterone we were unable to recover any pregnanediol from the urine. By continuing, however, we found that by the third treatment as a rule some pregnanediol would appear, and with subsequent treatments pregnanediol appeared in the normal quantity. This has been a regular finding with this disease and we have no explanation as to why this should be so. It would appear, therefore, that one of the features of this disease is the inability to deal with progesterone normally but that this disability is removed by substitution therapy.

More recently a substance, anhydrohydroxy-progesterone, has been discovered which has progestational activity when administered by mouth, but this activity appears to be about one-tenth weight for weight of injected progesterone. For obvious reasons it would be a great advantage if we could substitute this substance for progesterone, and I have, therefore, compared treatment of metropathia hæmorrhagica with progesterone and anhydrohydroxy-progesterone. In order to compare the results I first used ten times the quantity by mouth, administering 800 mg. over the course of eight days. At first it appeared to work well. The hæmorrhage usually appeared up to five days following cessation of therapy and this usually went well for several months, but at the end of such a period the condition frequently relapsed and progesterone had to be used again. By varying the dosage I found that the effect could be produced just as well with half the dosage and finally by a quarter the dosage, and the relapse rate was no greater with the small than the high dosage. In an endeavour to see whether even at ten times the dose of progesterone the dose was still inadequate I doubled it and gave a course of 1,600 mg. but even in this very large dose there was still a high relapse rate. There are a few patients who have been kept well for up to three years but it appears that slightly less than 20% of such patients can be kept permanently well by substitution therapy with this substance.

Examination of the endometrium has shown that by adequate dosage with progesterone, secretory endometrium is produced, but so far even with the very high dosage of anhydrohydroxy-progesterone full conversion of the endometrium has not been seen. In view of the experimental findings that œstrogen is necessary to prepare and hold the uterus for the action of progesterone, I have added small and large doses of œstrogen at the same time as the administration of anhydrohydroxy-progesterone but it did not appear to make any difference to the results, and the endometrium still remained unconverted.

[*June* 16, 1944]

Continuous Caudal Analgesia in Obstetrics

A Preliminary Report [*Précis*]

By A. H. GALLEY, D.A., and J. H. PEEL, F.R.C.S.

Dr. A. H. Galley said that neither Mr. Peel nor he claimed to have participated in the inception of *continuous caudal analgesia*, although they were probably the first to have employed the technique in the British Isles.

The investigation had been conducted in the Obstetric Department of King's College Hospital, London, with a view to ascertaining: (1) Any difficulties associated with the technique, the efficiency of the analgesia, and whether there were any untoward sequelæ. (2) Whether caudal analgesia modified the normal course of labour, and if so, whether such modification was in any way detrimental to the welfare of the mother, the fœtus, or both.

It was hoped to encourage informed criticism upon the subject, and, perhaps, to stimulate others to try the method for themselves, and thus widen the scope of the investigation.

ANATOMICAL CONSIDERATIONS

Dr. Galley reminded his listeners of the innervation of the uterus and birth canal, a study of which revealed that the pain of uterine contractions was experienced *via* the sympathetic system, and that a spinal nerve-root block up to and including the 10th dorsal segment would eliminate *all* painful sensations associated with parturition. It might also augment cervical dilatation by paralysing the motor pathway to the cervix uteri, a possibility which appeared to be borne out in practice. A block reaching higher than D.10 must be avoided, as it affected the sympathetic motor fibres supplying the upper segment, thereby diminishing the force of uterine contractions.

The extradural space surrounded the dural sac from the foramen magnum above to the sacral hiatus below, and was divided into two portions. The upper, or peridural, space was a potential cleft, but the lower, or epidural, space occupied the major portion of the sacral, or caudal, canal; the two were continuous. The dura terminated at the level of the 2nd sacral bony segment, and the rest of the epidural space was occupied by elements of the cauda equina, a venous plexus, and areolar tissue; sheaths of dura occasionally accompanied individual equinal nerve bundles, and might be pierced by a needle at a level considerably lower than the position of normal termination of the dural sac. This was rare but must be remembered.

The sacral hiatus, which gave access to the epidural space, was situated at the lower end of the dorsum of the sacrum, was covered by a membrane called the sacro-coccygeal ligament, and sandwiched between two bony prominences known as the sacral cornua. Both the hiatus and the two sentinel sacral cornua were very variable in size, and when it was recollected that superimposed upon this unpredictable anatomy was a varying thickness of the fat of pregnancy, it was obvious that the technique might at times present considerable difficulty.

TECHNIQUE

The object of caudal analgesia was to introduce an analgesic solution into the epidural space in such quantity that it would force its way up into the peridural space to the level of the 10th dorsal roots; all roots traversing these two spaces below this level would then be blocked. In continuous caudal analgesia, an innovation introduced by Hingson and Edwards, the needle was kept in situ within the epidural space, and additional doses injected from time to time in order to maintain an unbroken analgesia.

Dr. Galley proceeded to describe the technique of introducing the caudal needle (this technique is described in "Recent Advances in Anæsthesia and Analgesia", by C. Langton Hewer, Fifth Edn., p. 175). A lumbar-puncture type of needle of semi-malleable texture was considered the most safe. In order to avoid undue disturbance during delivery, the left lateral position had been employed while inserting the needle, and during analgesia. The following points had emerged during the investigation: Excessive infiltration of the skin and underlying tissues prior to insertion of the needle obliterated the anatomical landmarks and made it difficult to discover the sacral hiatus. If the needle were swung too far round after passing through the skin it might skid on to the dorsum of the

sacrum; the most common reason for failure to produce analgesia. Pressure over the skin wheal, while trying to introduce the needle-tip into the sacral hiatus, was often very efficacious. While performing the aspiration test in order to ensure that the needle-tip did not pierce the dural sac, or lie in the lumen of a blood-vessel, it was as well to introduce a minim or two of fluid before aspirating, in case the tip were clogged with a plug of tissue.

Once the needle was in position the course of analgesia could be divided into three: the precautionary dose, the main dose, and the topping-up doses. The precautionary dose was 8 c.c. of metycaine 1½% in saline, after which the administrator must wait for ten minutes to make sure that spinal analgesia did not occur, due to the needle piercing the dural sac. In the speaker's modest experience, no signs of analgesia had ever materialized after this injection if the needle were in the epidural position; should such signs occur, the injection should be assumed to be intradural ("spinal") and the method abandoned. In successful techniques (analgesia not having supervened) the precautionary dose should be followed by the main injection of 30 c.c.; disappearance of labour pains (as distinct from uterine contractions) should then follow in from fifteen to twenty-five minutes. Occasionally, islands of pain remained in such places as the uppermost thigh: very occasionally analgesia was much more marked on the dependent side; this could be remedied by turning the patient on to the other side and adding 20 c.c. The effect of the main injection varied, and lasted for anything from forty to eighty minutes, so that it was advisable to administer topping-up doses every forty-five minutes; these were best limited to 20 c.c. Metycaine 1½% solution had proved much more effective than procaine ("novocain", "planocaine") up to strengths of 2%. Metycaine was obtainable in powder form, and could be made up in any hospital dispensary, autoclaving the resultant solution in the usual manner.

APPARATUS

Dr. Galley then described the various forms of apparatus that had been tried during the investigation. The injections could be made quite simply by connecting the syringe directly to the needle. There was a great deal to be said, however, for a system of remote control, allowing the analgesic solution to be sucked from a reservoir into the syringe, and diverting it, via the medium of a valve, along a length of tubing attached at its far end to the needle. Recently Messrs. Eli Lilly & Co. had kindly obtained a replica of the latest apparatus made for Drs. Hingson and Edwards by Becton, Dickinson & Co., of Rutherford, N.J., U.S.A. This consisted of the famous Luer-Lok syringe, valve, and needles, and the latest malleable caudal needle. The needle could be straightened after use by rolling it between the finger-tips and any hard, flat, surface; and the malleability greatly reduced the risk of fracture.

MODIFICATION OF TECHNIQUE FOR ANALGESIA DURING CÆSAREAN SECTION

It had been found that larger volumes of analgesic solutions were required to produce skin analgesia than to ensure sympathetic block; for instance in Cæsarean section following trial labour, labour pains were obtunded at a point when analgesia had barely reached the pubis, and even when the required sensory block was effected, the motor block was minimal. Such a difference in the sensitivity of the various components of the nervous system to analgesic drugs was well recognized in spinal analgesia (intradural block), but the effect was much more telescoped and therefore less obvious. Metycaine 1% had been employed to minimize the likelihood of precipitating toxic symptoms with the large volumes used. The precautionary dose was raised to 10 c.c., the main dose to 40 c.c., and topping-up dose of 30 c.c. given every ten or fifteen minutes until analgesia (to pain, not touch!) reached the desired height. The method was time-consuming, but had been employed successfully in cases of heart failure and diabetes.

PITFALLS AND DIFFICULTIES

The surface markings associated with caudal analgesia were sometimes obscure, especially in the obese. The technique suffered greatly from the lack of any positive indication that the needle was correctly placed; one missed, for example, the appearance of C.S.F. as in a successful lumbar puncture. Once pierced, the dura must be considered able to admit any quantity of fluid introduced into the epidural space, thereby producing spinal analgesia. In one such case the speaker had proceeded cautiously, and produced analgesia up to a height of D.8, with as low a volume as 11 c.c. metycaine 1%, even after the needle had been withdrawn nearly ½ in., and an aspiration test had proved negative!

Had the 90 to 130 c.c., usually required in caudal analgesia, been introduced disaster might well have supervened!

The needle might easily slip to one or other side of the root of the coccyx, or even traverse the sacro-coccygeal joint space, to burrow amid the perirectal tissues. If withdrawn and reinserted, the needle might carry infection with it. Beginners were apt to prod about unnecessarily and devitalize the tissues in the adjacent area; this occasionally produced a shallow skin necrosis resembling a miniature bed-sore, which usually appeared within forty-eight hours of injury; it had always responded to treatment with sterile talc and spirit. In one unfortunate case, a buttock abscess had developed three weeks after an unsuccessful administration, but it was not certain whether this was caused by a breakdown in the aseptic technique, or to the pointing of a pelvic cellulitis consequent upon a severe tear in the posterior vaginal wall which had been overlooked by the house-officer conducting the delivery. Opinions were still divided upon the causation.

CONCLUSION

Dr. Galley concluded by saying that both Mr. Peel and he felt certain that failure to produce analgesia was due to faulty technique; all failures submitted to X-ray had been found to have the needle misplaced. Successful analgesia was usually complete, and far superior to anything as yet employed in obstetrics. The technique was probably more difficult than lumbar puncture, but as with most skilful procedures, practice and perseverance had been attended with an increasing measure of success; the fact that there had been ten failures in the first thirty cases, and only two in the next thirty, suggested that their technique was improving.

Mr. Peel said that in order to gain experience in the technique and learn more about this method of analgesia they employed it for cases where the analgesic effect would only be required for a relatively short time, and accordingly started by using the method for Cæsarean section and for the relief of pain during the second stage of labour.

The first group comprised the bulk of the cases where caudal analgesia had been given primarily for the relief of pain. There were 39 such cases—23 of them primigravidæ, 16 multigravidæ. The effects of a successful caudal analgesic on the course of labour were as follows: Usually within ten to fifteen minutes the pain was completely relieved. The patient, having been in distress with each uterine contraction, became relieved of all pain. When the effects of the analgesic had become fully manifested the continuance of uterine contractions could only be appreciated by palpating the uterus. Sometimes the patient was conscious of a contraction; she felt a sensation of movement in the front of the abdomen, but in a large number of cases she had been unaware even of such a disturbance. Usually the relief of pain manifested itself first. After this cutaneous analgesia gradually developed commencing in the perianal skin. The anus and perineum slowly became lax and patulous as well as analgesic. Rectal examination was rendered easy and painless. This laxity of the soft tissues was very characteristic. One of the earliest signs that the caudal injection was working had often been the involuntary escape of small amounts of fæcal material or residual enema fluid from the anus. Gradually the patient experienced a sensation of numbness in the legs, although usually she retained the capacity to move them.

When the injection was given after the second stage had become established, the patient, usually tired after the first stage, welcomed the relief to such an extent that she ceased to be at all co-operative. She had to be told literally when a contraction occurred and encouraged to bear down. The word "pain" had to disappear from their obstetric vocabulary. The weakness of caudal analgesia at once became apparent when employed deliberately and merely for the second stage of labour. The patient lost all desire or inclination to push, and when made to do so her efforts were undoubtedly not so efficacious. This had mattered little in the case of the multipara and all but two delivered themselves spontaneously. The ease with which the child almost glided out was sometimes quite remarkable, the tissues unfolding and stretching very easily. However, in the case of the patient having her first experience of labour, the voluntary muscular efforts were not as good as the involuntary bearing down in unrelieved labour. Forceps had consequently been necessary on some occasions.

The extreme laxity of the soft tissues made a low forceps extremely easy. The incidence of perineal tears was low, and they were much easier to repair because the tissues were so lax and the bleeding so much less.

Caudal analgesia was next used during the first stage. In 21 cases they had started when the dilatation of the cervix was from one shilling to half a crown. The effects

during the first stage had been uniformly excellent, excluding 3 cases where the needle had failed to enter the sacral canal. The patient might fall asleep especially if she had been given a very mild sedative. There was apparently acceleration of the first stage of labour. In all cases where good regular contractions had become established before the insertion of the needle completion of dilatation had occurred very quickly. In one case there was no dilatation of the cervix during four hours in spite of the presence of good contractions, the os remaining at one finger dilatation. Following the commencement of caudal analgesia the first stage completed itself in rather less than five hours. A caudal block might prove to be the best treatment for this type of case whatever its future might be for other purposes.

Mr. Peel went on to say that, therefore, it was obvious that the first stage of labour proceeded normally in every respect. The cervix, so soft and patulous, seemed to melt away very quickly in the hour or two before dilatation: the stage of labour which was most difficult to relieve by any other method. However, apart from some rectal pressure during a contraction, the typical physical signs which manifested themselves at the onset of the second stage were somewhat obscured. The membranes seldom ruptured spontaneously, and full dilatation frequently could only be diagnosed by rectal or vaginal examination.

All sedative drugs employed for the relief of pain had the following points in common:— They all diminished the force of uterine contractions and slowed down labour; they were all potentially dangerous for the baby; they all increased the risk of post-partum hæmorrhage and increased the incidence of forceps delivery in the second stage, and finally gave only a very partial relief to pain. In successful caudal analgesia the pains of labour were not only relieved but abolished.

There were 11 cases in which it had been impossible to insert the needle into the sacral canal. However, Mr. Peel said, their technique was improving. In a few cases the needle having been inserted, the initial injections had brought complete relief from pain but further injections had less and less effect whilst the cutaneous analgesia had persisted as well as the laxity of the perineum and pelvic floor. As a result the forceps were applied without pain, although the patient was still feeling some considerable pain with each uterine contraction. It was possible that as the force of the uterine contractions became stronger, the injected fluid did not diffuse upwards in sufficient concentration completely to knock out the nerve roots originating in the lower dorsal segment. Apart from these two or three cases they had had complete success in the first stage of labour. They intended to limit the use of caudal analgesia during the first stage of labour to cases that were obstetrically normal until further experience was gained.

In the case of the multigravidæ the analgesia might be carried out during the second stage when a spontaneous delivery could be anticipated. In the case of the primigravidæ, however, it seemed that the degree of analgesia should be lessened so that the patient could co-operate in helping to deliver the baby herself. There was no tiredness, weariness or exhaustion by the time the second stage was reached. If it were explained to the patient what she had to do during the second stage, she would be in a far better mental and physical condition when the contractions were allowed to become painful again. If for purely obstetric reasons forceps became necessary, then a further injection would abolish pain and produce analgesia sufficient to enable forceps to be applied.

Caudal analgesia seemed to have no ill-effects on the baby. In all the cases, with three exceptions, the baby cried spontaneously and immediately. The three stillbirths had all been due to obstetric reasons, and could not be attributed to the caudal injection.

Of the third stage of labour, Mr. Peel said that while analgesic drugs and general anæsthetics all predispose to a more free loss of blood, every single third stage with caudal analgesia had been completed with minimal blood loss and with fewer perineal lacerations to repair.

CAUDAL ANALGESIA FOR FORCEPS DELIVERY

The majority of primigravidæ who had received caudal analgesia for the relief of pain in the second stage had to be delivered by forceps which was obviously a disadvantage, although the forceps delivery itself was very easy. But it occurred to Mr. Peel that a very definite place could be found for caudal analgesia in cases where other methods had been employed for relieving pain in the first and second stage, and yet forceps had become necessary. The commonest indications were uterine inertia, occipito-posterior position of the occiput and slight degree of contraction of the pelvis. Caudal analgesia was ideal for such cases. Relaxation of the pelvic floor and perineum made rotation, if necessary,

easier, as well as the application of forceps. A similar degree of relaxation using general anæsthesia could only be attained by inducing a depth of anæsthesia that would add to the shock and at the same time diminish the force of uterine contractions. With general anæsthesia post-partum hæmorrhage was a common sequence. With caudal analgesia the force of the uterine contractions was not further reduced and this risk of post-partum hæmorrhage was minimized. Anæsthetic dangers to the baby were avoided. Their results in employing caudal analgesics this way had been most impressive. Usually a single injection of 40 c.c. of metycaine had given the necessary analgesic effect in their cases, although if the needle were left in situ, an additional 20 c.c. might be injected immediately before the application.

Mr. Peel had not yet conducted a breech delivery under caudal analgesia, but there should be no contra-indication to its use. It was clearly not a good method to employ for such intra-uterine manipulations as internal or bipolar version.

CAUDAL ANALGESIA FOR CÆSAREAN SECTION

Their experience with caudal analgesia employed for Cæsarean section had been on the whole satisfactory apart from a few failures due to failure in technique. Of late years many obstetricians avoided general anæsthesia for this operation—using instead local analgesia or spinal anæsthesia. The advantages of caudal analgesia compared with local analgesia were: The injection of a large quantity of fluid at the local operation site was avoided; the degree of pain relief was much more complete; stretching of the parietal peritoneum, which was frequently painful when local analgesia was employed, was quite free from pain. Further, caudal analgesia could be employed when Cæsarean section became necessary at the end of a trial labour. Local analgesia was unsuitable for such cases. Caudal analgesia abolished the pain without interfering with the contractions.

Spinal anæsthesia carried with it certain well-known disadvantages and dangers (spinal headache, 6th nerve palsy, meningitis and occasional residual pareses), especially when employed for Cæsarean section. Caudal analgesia acted as a regional block and as such it was definitely superior in its results to purely local analgesia.

CONCLUSIONS

From their experience, Dr. Galley and Mr. Peel both thought caudal analgesia the best method of producing analgesia for the performance of Cæsarean section and for forceps deliveries; that it was an unqualified success in relieving the pains of labour in the multigravidæ throughout labour; but in the primigravidæ a modification in technique must be established before it could be accepted as the ideal way of relieving pain during the second stage. Its disadvantages were threefold: First, a difficult technique; secondly, a considerable call on the time and patience of the obstetrician or anæsthetist or both; thirdly, some patients were psychologically unsuited to any form of local or regional analgesia.

They extended their thanks to Messrs. Eli Lilly & Co. for the loan of the apparatus; to Sister Alison and Sister Freda at King's College Hospital for their co-operation and help; to Miss I. C. Barne, their Registrar for her assistance on many occasions, and to Mr. Gilliatt for his interest and encouragement.

Section of Ophthalmology

President—F. A. JULER, F.R.C.S.

[*June 9, 1944*]

Left Retinal Lesions.—MAURICE WHITING, O.B.E., F.R.C.S.

Girl aged 15; came to hospital on March 29 complaining that the sight in her left eye had been deteriorating during the past two months. Her vision was 6/18 in each eye, and in the left eye she had some small white spots aggregated along the inferior temporal vessels and between the superior and inferior temporal vessels around the macular area (fig. 1). The opinion of one colleague was that it was a retinopathy with a
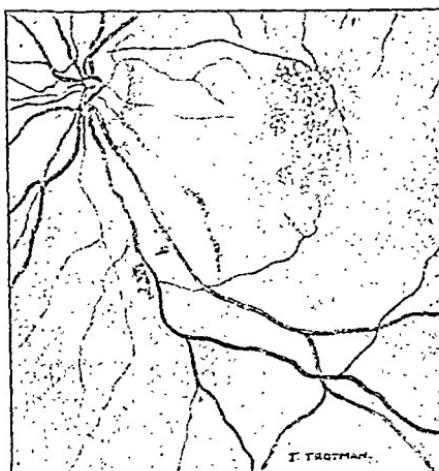
FIG. 1.—Left retina, March 29. White spots round macula and along inferior retinal vessels. Retinal œdema.

FIG. 2.—Appearance in May, when spots have mainly cleared up, leaving an area of retinal degeneration along the inferior temporal vessels.

OCT.—OPHTH. 1

vascular basis; of another that it was probably allied to Coats's disease, and of a third that it was an old vascular lesion. The Wassermann was negative, and there was no real clue to the cause of the condition.

The disappearance of the white spots had occurred in the last few weeks and had left only a slight patch of degeneration below (fig. 2).

The President asked whether it was a retinal or a choroidal condition.

Mr. Whiting replied that the distribution and the œdema associated with retinal vessels made one think it was primarily retinal.

The President considered that it might have been a superficial exudative choroiditis, with a secondary œdema affecting the retina extensively.

Retinitis Punctata Albescens.—HUMPHREY NEAME, F.R.C.S.

Elsie G. aged 36, applied at Moorfields Eye Hospital for a certificate for relief from fireguard duties on account of night-blindness. She stated that she had been to hospital at the age of 8 or 9 years with this complaint. Her parents were first cousins, but neither of them was affected. She had no knowledge of this defect in any of her grandparents or uncles or aunts, but said that a brother and two sisters were night-blind. The brother had three boys none of whom had night-blindness.

With lenses the vision of the right eye was (27.5.44) 6/12, 6/9 (5), and the left 6/24, 6/18 (2). The pupils were equal and active and the eyes free from signs of inflammation. Both eyes were examined after pupil dilatation with homatropine and cocaine. The media were clear. Both fundi showed discs of healthy appearance. In both there were very numerous pale spots, oval or circular in shape, of size about equal to the diameter or × 1½ diameters of a main retinal artery. They were most numerous in a band corresponding roughly with the circumference of a semicircle to the temporal side of each macula, extending above and below the disc. A few only were seen to the nasal side. Some of the spots were partly covered by retinal arteries, which crossed anterior to them. Peripheral to this area, in the intermediate zone, were numerous small pigment deposits in the form of dots and short rods. In some parts were denser aggregations of pigment spots of similar form. Towards the temporal periphery in the right eye was an oval area where the large choroidal vessels and intervascular choroidal pigment were more clearly seen as though superficial choroidal atrophy had taken place, with some increase of pigmentation peripheral to this. There were other smaller ill-defined areas of choroidal pallor, but nowhere any typical indications of previous choroiditis. The fundi for the most part were of slightly albinotic type.

The field of vision of the right eye was irregularly contracted and everywhere within the 42° circle (1° white object, in the darkroom with the Lister illuminated perimeter). There was no nystagmus, nor were there any stigmata of congenital syphilis, in teeth (only the lower incisors remained), nose, frontal bones, nor any history of bone or joint affections. Hearing was good. Wassermann reaction negative (Moorfields Eye Hospital).

Mr. O. Gayer Morgan said that he saw a case the other day in a child aged about 10 with a fundus almost exactly like the one shown by Mr. Neame. She was sent up because she was found to be night-blind at school. She was investigated thoroughly but results were negative. There was a kind of stippling all over the periphery of the fundus. He also examined two of her younger sisters not yet at school, and found their fundi to be the same. The mother had written him later to say that she was now quite certain that the elder of these two was night-blind. The parents were not related, but one of the mother's brothers, who was a child of cousins, was night-blind.

Left Central Retinal Lesion.— V. M. ATTENBOROUGH, D.O.M.S.

Mrs. Attenborough said that the patient was first seen at Moorfields in February 1943. He complained of gradual loss of vision in his left eye. His right vision was then 6/6 and his left 6/18. On examination he was found to have some fine pigmentary disturbance at his left macula. In June 1943 his left vision had improved to 6/12. He did not attend hospital again until May 1944 when his left vision was found to have fallen to less than 6/60. On examination the appearance of the left retina was as shown in the illustration. There was a raised mass on the temporal side of the left macula, and some pigmentary disturbance and œdema of the macula itself. The Wassermann reaction was negative; report from the Ear, Nose and Throat Hospital negative; urine normal; blood-pressure 150/95.

In view of the fact that the patient was only 49 years of age Mrs. Attenborough asked for opinions as to whether the mass was inflammatory, degenerative or neoplastic in character.
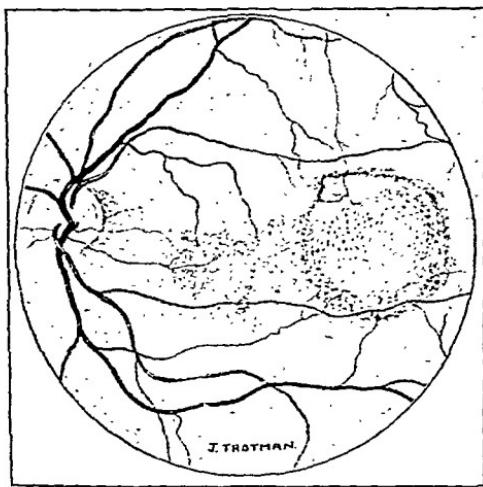
Central retinal lesion in patient aged 49.

Mr. O. Gayer Morgan said that the drawing made it appear that it was a much more solid thing than was actually the case. It looked to him much more cystic. If there was some central vision it might be almost worth while carrying out a puncture.

Mr. Humphrey Neame said that he thought the case looked rather more homogeneous than was represented in the drawing. It appeared to be of a very pale milky colour, definitely bulging, and reminded him of an earlier stage of a case he had a good many years ago in which a swelling at the macula was thought possibly to be an early leuco-sarcoma of the choroid. It did not, however, grow as one expected a sarcoma to grow, and after eighteen months some small pale spots were seen in the macular area of the other eye and the vision steadily deteriorated.

Mr. C. B. Goulden said that the appearance in the macular region reminded him of that seen in an eye with very massive retinal exudation.

Left Macular Coloboma.—VICTOR PURVIS, M.B.

Girl aged 14. Was discovered at Moorfields in routine examination seven years ago to have coloboma. There was a large punched-out, circular hole of approximately three discs in diameter with pigmented, overhanging margin, and a slight degree of pigmenta-tion in the floor of the colobomatous area. No retina was to be seen in the coloboma. There were a few large choroidal vessels passing diagonally across the floor. The parti-cular point of interest was the extreme ectasia, which he had never previously seen so marked in a coloboma that was lined by choroidal tissue. The case appeared to fall between the first and second groups of Miss Mann's classification. The characteristic gross visual defect was present, vision being only 6/60, with eccentric fixation. There was no relevant family history, and if one agreed with the intra-uterine inflammation theory of the origin of the condition this coloboma presumably had a choroiditis as the retinal vessels were forming in the fourth or fifth month. The right eye was normal; vision = 6/5.

The End-Results of Operation for Detachment of the Retina (with a Follow-up of Fifty Successful Cases).—MONTAGUE HINE, F.R.C.S.

Mr. Hine gave a full analysis of the results of operation in 120 cases which were done at his E.M.S. base. They were completed by November 1942, so that sufficient time had elapsed to determine the final result in the 50 successful cases. He pointed out that, after excluding a group of 49 cases from one source, in which there was a high percentage of unfavourable risks (30·6% successful) the average figure for success could be taken at practically 50% for unselected hospital cases, obtained from many sources. He pointed out the danger of compiling statistics too early, several cases relapsing after periods up

to six months, and a smaller number proving satisfactory only after an interval of several months.[1]

This paper, in full, is being published in the *British Journal of Ophthalmology*, November 1944.

Mr. J. Cole Marshall desired to say how much he appreciated what Mr. Hine had done for him, especially in the bad cases he had sent him. What he admired specially about his paper was his consummate honesty. It was quite refreshing to hear a man speak as he did about his cases. He knew what trouble he took over them. After hearing Mr. Hine he still felt inclined to stick to his old method because he was quite certain that the separate needle method did *not* do so much injury to the vitreous as the surface coagulation method. If one was going to cover a large area to try and cure a detachment he did not think the eye was damaged so much by making a barrage with various sizes of needles. One case which he saw recently was operated on by Sir John Tweedy forty years ago for needling of a left congenital cataract. The man came to him with detachment on the nasal side of the retina, and he still had at the time he saw him a vision of 6/9. He found he had cataract in his right eye, and, knowing how difficult these cases were, he determined to do an extraction in the right eye before he did anything in the left eye, which was the eye originally affected. Much to his surprise, the patient allowed him to do the left eye, and he was glad to say that the result had been quite good; he had got 6/18 vision. A barrage was made from "12 o'clock" to "7 o'clock" with a 1 mm. needle. The current was about 45 ma. That was 18 mm. from the ora. Another barrage was made 14 mm. from the ora, and that let out the fluid; there was no need to use any other procedure for doing so. He was able to show a drawing of this case from which it could be seen what comparatively little damage these punctures had made (*see illustration*). At the top, there was a typical coagulation
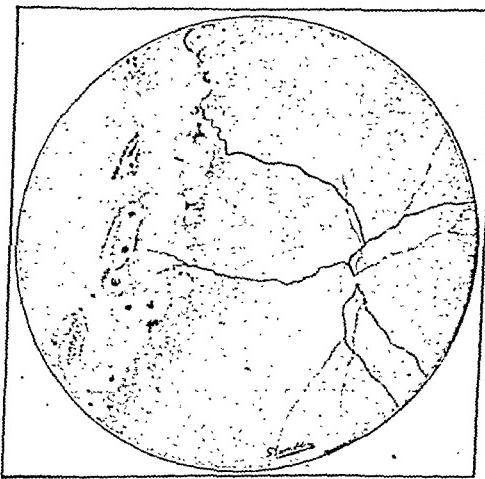
Fundus in an aphakic eye showing the result of a double barrage with 1 mm. and 1½ mm. needles. *No hole was found in this case.*

with some pigment. This was an operation he felt was often useful for a difficult class of case. In some of these cases a second and third (even in one case a fourth and a fifth) operation was necessary, and the eye stood the operations very well. The operation carried out might be termed the Lindner Safar operation, with various lengthed needles, though Weve of Utrecht claims he first used a perforating needle to let the fluid out of a detachment after he had done a surface coagulation.

[1] He stated that of fifteen patients in the series who had originally been seen privately, ten were included in the list of successes, or 66·6%. Three of these cases had vision 6/6, and two 6/9, very much better than the average vision of the rest of the group.
Thirteen of the series had had detachment in the fellow eye, i.e. 10·8%. Seven were successful.
Twenty had secondary operation. Only three were successful, and two of these had fresh holes in another sector of the retina.
There were four cases of *aphakia*. None was successful, but a more recent case had held for nine months.
Myopic cases were 40%. Under − 6D successful nine out of nineteen, − 6D to − 12D successful eight out of twenty. Over − 12D successful none.
Traumatic cases were seventeen, or 13·83%. Successful nine. Practically all the rest had most unfavourable factors.
Multiple retinal holes present in eighteen cases. Six successful.
Localized "moth-eaten areas" three cases, all successful.
No hole or disinsertion in six cases. Only one successful.
Mr. Hine concluded that neither the age of the patient, in itself, nor the position of the hole, was the determining factor in success, which largely depended on the state of the retina. It was not fair to give too rosy a prognosis to patients with high myopia, extensive retinal degeneration, multiple holes or aphakia. A few of the promising cases ultimately proved unsuccessful, but some of the very unpromising ones turned out to be successful. There were very few who should not be given the chance of operation, provided they were willing to accept the odds.

Mr. C. B. Goulden, after expressing appreciation of Mr. Hine's work, said that an interesting point which had come out of his paper was that his private cases did the best. That was the usual experience because these cases tended to come early, and early operation was of the greatest possible importance. He supposed one ought to be able to cure every case of disinsertion. Mr. Hine had not done so, and therefore he supposed it was not always possible, but the cases did give an excellent prognosis.

One comment about the classification of cases. He did not think it was a fair estimate of the value of the operations for detachment to bunch them all together, any more than it would be to bunch together all cases of appendicitis. One was sure with regard to certain cases of appendicitis when they came to one, that they were going to die soon, and to mix these up with cases of quiet appendicitis was not fair. The better dissection of these cases was really necessary. Mr. Hine would possibly have done better to have put together all his cases of disinsertion which had a good prognosis, all those in which the prognosis was obviously bad, and all those in which there was some sort of chance of curing the patient. He thought that ought to be done in the future. It would give the operation a better name and would give more hope to patients. He did not think it was appreciated how often detachment followed extraction for cataract, not only in early life, but after senile cataract. It was extraordinary how often detachments had occurred in cases of zonular or lamellar cataract, and the regularity of such occurrence after a space of twenty-five years. It was interesting that it seemed to follow that time-table.

Mr. Hine had mentioned that all those cases which had detachment after extraction had had a discission. That might lead one to think that a discission had something to do with the detachment. But he had seen cases of detachment in which a discission had not been done. He recalled a case of his own which came back for discission a couple of months or so after extraction, when the retina was already detached. It was puzzling why detachment did occur so frequently after extraction of cataract. He had seen detachment occur in both eyes after extraction in both eyes. He thought of two tragic cases of his own in which subsequent operation for detachment was of no value.

The point made about having a properly working machine was of great importance. Mr. Hine had said that the machine which came to him came with an electrician. One cause of bad results was that there was not always attached to the hospital a man who could keep the machine in proper order. One had had the experience of being about to operate on a case and then finding that the machine was not what it should be; if the conjunctiva was reflected at that time one could not very well turn back, but must go on as well as one could.

Mr. Victor Purvis asked the proportion of disinsertions in the thirteen bilateral cases; and mentioned that in regard to secondary tears (that is tears developing at the edge of the reaction) he was under the impression that they were due rather to a current that was too strong than to a retina that was too fragile, but he agreed that usually the prognosis of these secondary tears was bad.

The President asked whether trouble had been encountered in connexion with reaction. Of two cases on one afternoon during the previous week, in one a beautiful reaction was obtained with a current of 95 ma., but in the second case no reaction was obtained, even though the apparatus was pushed up to 150 ma.; nor did any effect appear later.

Dr. T. H. Whittington said that there were a certain number of cases in which the retina was re-attached successfully, but the patient could not see because of severe hæmorrhages or exudates into the vitreous.

Mr. Montague Hine said that on five or six occasions he had had cases in which there had been no reaction at all. On the same morning, of two cases which appeared to be exactly the same, one would show a reaction and the other not. He had found that three cases which showed no diathermic reaction on the operating table ultimately showed a good deal of very fine pigmentation and did very well.

He had not noticed the falling off in the reaction. That, however, was probably because, unless there were multiple holes, having made his first observation and seen the position of the first reaction, he did not keep on looking at it as the operation proceeded.

In reply to Mr. Purvis two of the seven successful bilateral cases had disinsertion and one of the six unsuccessful cases.

In reply to Dr. Whittington, there was, he felt, a certain danger of overdoing things and getting a "building-up" reaction. For his own part he was more afraid of over-doing than of under-doing. Most of the patients in whom he had seen much vitreous opacity after operation were very high myopes and he supposed they got choroidal and retinal hæmorrhages and effusions.

The Removal of Malignant Tumours of the Iris

By F. A. JULER, F.R.C.S.

MALIGNANT tumours of the iris may be pigmented or non-pigmented. It has been well established that the former usually originate in pigmented nævi of the iris. This has been shown by Collins (1926), and cases have been reported by several authors (Mayou, 1930; Neame, 1942; Black, 1942).

Cases of leucosarcomata are rarer, and have been collected by Duke-Elder and Stallard (1930), but apart from the absence of pigment they do not seem to differ in histology or malignancy from the more usual malignant melanomata: they often show looped vessels on the surface.

A ring sarcoma of the iris has also been described, which infiltrates the tissues in preference to the more characteristic nodular formation, and which is likely to have spread beyond the iris structure.

The malignant melanomata of the iris are relatively mild in their degree of malignancy, and several cases of local removal have been reported in this country, whilst the indications have been discussed by both Neame and Black, who have had successful results.

In 1936 I showed before this Section a case in which local removal was later undertaken (Juler, 1937). It was a localized nearly flat growth of the iris in a man of 70 years, and there was no difficulty in removing it by iridectomy. The anterior chamber was of average depth, and a sufficient section was easily made with a Graefe knife, whilst the limitation of the tumour to the pupillary half of the iris relieved anxiety about any incomplete removal from the base. The iris was gripped at the side of the swelling, and the mass extruded easily.

I saw the patient five and three-quarter years later, when no recurrence was present: visual acuity had previously been 6/6 partly, and was then a little worse (6/9 with 6/6 partly), owing to the progress of lens opacity which had already been noted as present before the operation.

I am now able to report a further case, and suggest a method of removal which seemed appropriate.

On June 18, 1942, A. R., male, aged 37, gave the history that he had been aware of a brown mark in his left iris for some twenty years, and that it had slowly got larger during the last few years.

Each eye had 6/6 vision.

In the left iris, there was a tumour projecting from the surface of the sector between 12 and 2 o'clock (*see* fig. 1). It included the whole width of the iris, overlapping the
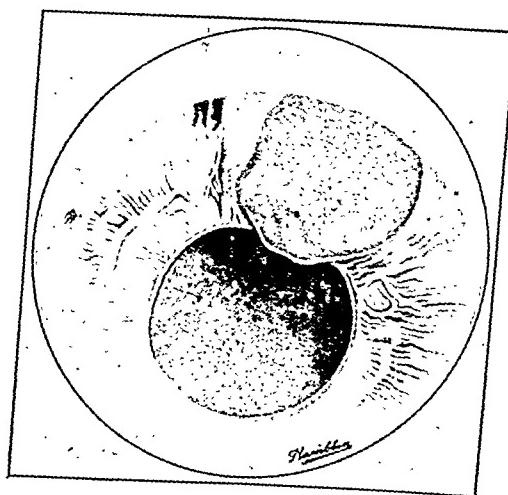
FIG. 1.

pupillary margin, and just disappearing from view behind the limbus. Its outline was roughly circular, and, although the periphery towards the ciliary region could not be seen, the curve of the circumference suggested that it did not extend beyond the iris proper. Its surface was of a dark brown colour, smooth for the most part, with a few depressions here and there: no blood-vessels were visible on its surface. There was no apparent tumour of the posterior surface or of the ciliary region. The front of the tumour was separated from the cornea by a thin layer of fluid. The rest of the iris was of grey colour, save for a few small pigmented spots. The tension was normal, the cornea clear, and the eye free from inflammation.

Of opinions expressed by my colleagues at Moorfields, four were in favour of removal by iridectomy, two were for excision.

In devising a method for local removal two factors were important. (1) The proximity of the tumour to the cornea precluded the use of a Graefe knife or a keratome in the affected sector on account of the danger of cutting the swelling. (2) The peripheral limit indicated a removal at least as far as the iris base.
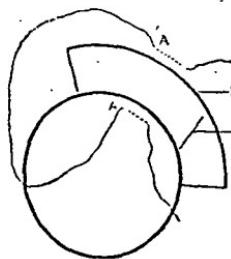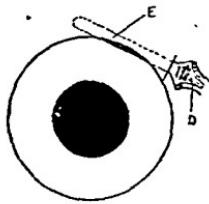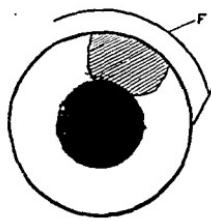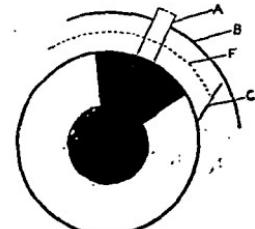
FIG. 2.   FIG. 3.   FIG. 4.   FIG. 5.

On June 29, 1942, under local anæsthesia a sclerocorneal suture was inserted (A) and a flap of conjunctiva was dissected to the limbus (B). With a small keratome an incision was scratched in the sclera radially from the limbus along the 2.30 meridian over a length of 2·5 mm. (c): this was made obliquely, sloping in an upward direction until the anterior chamber and ciliary body were reached. A Sinclair cyclodialysis separator (fig. 3, D) was introduced along the periphery as far as the 12 o'clock meridian, and was pressed well into the angle (E). The sclera was then incised by cutting down on the separator with a Beer's knife (fig. 4, F).

To remove the tumour an unsuccessful attempt was made to catch the iris margin with a blunt hook, both laterally and mesially. By means of iris forceps applied to the outer side, however, the tumour protruded readily and was abscised (fig. 5). Some pigmented tissue in the wound was also removed, and histologically was found to consist of normal ciliary processes. Healing was uneventful.

On July 17, 1944 (twenty-four months after operation), the visual acuity of the operated eye is 6/9, improving with cyl. − 1·5 ax. 20 to 6/6 (5). The eye is quiet, there is a slight subcapsular opacity of the lens opposite the centre of the iris coloboma. The tension is normal and there is no evidence of recurrence. Examination with the gonioscope reveals normal ciliary processes, and no abnormal pigmentation in the region of Schlemm's canal. With the corneal microscope a slight deposit of pigment on the lens equator at 1 o'clock and a small pigmented sphere on the iris at 4 o'clock have been noted as unchanged for eighteen months.

The Histological Report

The preparations owing to kinking of the specimen and to wartime deficiencies leave much to be desired. The tumour contains well-formed spindle cells with a considerable amount of collagen and some reticulum formation. The cells are spreading into the iris stroma without a definite capsule, and in places are heavily pigmented. No mitotic figures are seen. It is impossible to say whether removal has been complete.

Comment.—The method of removal described above seemed to offer a good prospect of removing the affected part of the iris to the extreme periphery, and indeed by this method I believe that a sector of the ciliary body might also be ablated, although naturally the suspensory ligament of the lens would sustain partial damage.

In his case Black had to deal with a somewhat similar proposition. He made a keratome section to the side of the tumour where the chamber was free, and enlarged this around the iris base with scissors. His result was satisfactory.

It is worth while to collect the indications which point to (1) malignancy of an iris tumour (2) to the possibility of removal by iridectomy.

(1) *Malignancy* will be indicated by a history of increasing size, a definite non-translucent protrusion from the anterior or posterior surface, and the absence of inflammatory signs.

Increase of tension also points to malignancy, and is suggestive of extension to the canal of Schlemm.

Flattening of the pupil and loss of its mobility may be suggestive, but a notch in the pupil is not definite evidence, for I have notes of another case in which a notch was present, although the size of the iris melanoma in relation to it did not alter in fourteen months.

(2) *Local removal.*—Extension may be insidious to the ciliary body, the corneal periphery, or the retina. The gonioscope should be useful in excluding extension around the angle on to the corneal periphery, where some abnormal pigmentation might be seen: for this examination it would be necessary that the tumour did not fill the anterior chamber sufficiently to obscure the view through the gonioscope.

Increase of tension would be a definite contra-indication to local removal as also would any evidence of ciliary involvement. It has to be remembered that incomplete removal may produce rapid filling up of the eyeball with growth, as in a case described by Greenwood (1929), in which extension soon involved the eyelids.

The therapeutic application of *radium* as an alternative or additional measure has to be considered. It is unlikely that the slow-growing spindle cells found in these cases are likely to be radio-sensitive. Doses would have to be severe and damage to the eye would be likely to accrue. Neame applied it in one of his cases as a treatment after iridectomy. A 5 mg. plaque was applied for one hour on two occasions, and considerable discomfort occurred up to three years later. Stallard (1933), on the other hand, states that intra-ocular sarcomata are very sensitive and he reports a good result.

REFERENCES

BLACK, G. W. (1942) *Trans. Ophthal. Soc. U.K.*, **72**, 304.
COLLINS, E. TREACHER (1926) *Trans. Ophthal. Soc. U.K.*, **46**, 86.
DUKE-ELDER, W. S., and STALLARD, H. B. (1930) *Brit. J. Ophthal.*, **14**, 158.
GREENWOOD, A. (1929) *Arch. Ophthal. N.Y.*, **1**, 650.
JULER, F. A. (1937) *Proc. R. Soc. Med.*, **30**, 701.
MAYOU, S. M. (1930) *Brit. J. Ophthal.*, **14**, 154.
NEAME, Humphrey (1942) *Trans. Ophthal. Soc. U.K.*, **72**, 103.
STALLARD, H. B. (1933) Radiant Energy, *Brit. J. Ophthal.* (supplement VI), 60.

Mr. Humphrey Neame said that these were uncommon tumours and well worth describing. He added a word about a case of his recently in which the eye had to be excised. It was one of extensive dendritic ulcer of the cornea and pigmented tumour of the iris. The growth was found in section not to extend to the angle, and by Mr. Juler's method the eye might have been retained.

Mr. C. B. Goulden said that some years ago he had a case of localized malignant growth in the iris. Removal took place by the free method of glaucoma incision. The notching of the pupil was an extremely important point. He was able to remove the tumour by making an incision such as one would make for cataract, seizing the healthy iris on one side, and pulling out just as much as if one was doing a large glaucoma iridectomy.

Mr. Humphrey Neame pointed out that the pupil was not absolutely circular in some cases of corpus nigrum of the iris. It was quite possible that the pupil might be congenitally irregular as in Mr. Juler's case. He recalled a case of secondary carcinoma of the iris, which was extremely rare, where the primary was not discovered. He lost sight of that case, but there was an extraordinary epithelial growth in the iris, and for a long time there had been a marked ectropion of the uvea.

Section of Experimental Medicine and Therapeutics

President—R. D. Lawrence, M.D.

[*June* 13, 1944]

DISCUSSION ON THIOURACIL AND THIOUREA IN THE TREATMENT OF THYROTOXICOSIS

Professor H. P. Himsworth: In May of last year E. B. Astwood (1943) reported the beneficial effects of treating cases of thyrotoxicosis with either thiourea or thiouracil. His claims, as far as they concerned the initial effects of these drugs, were soon confirmed on small groups of cases by Williams and Bissell (1943) and by Himsworth (1943). The purpose of this communication is to report the results of more extended experience.

When the treatment was first used in this country only thiourea was available but later thiouracil was obtained. The action of both these drugs on thyrotoxicosis is similar but thiouracil has distinct advantages over thiourea in not producing the unpleasant smell in the breath, the conjunctivitis or the vomiting which frequently attend the use of the latter preparation. These advantages quickly led to the exclusive use of thiouracil and in this paper, unless otherwise stated, the results have been obtained with that drug.

During the last ten months 33 cases of thyrotoxicosis have been treated by one or other, or both, of these drugs at University College Hospital. 26 of them were under my direct care and 22 of these have been observed beyond the period of initial treatment. The longest period of observation is ten months, the shortest ten weeks. Of these 22 cases, 7 were treated initially with thiourea and subsequently with thiouracil, the remaining 15 with thiouracil throughout. For convenience of discussion the results will be considered under the headings of initial treatment, maintenance treatment, symptoms of overdosage and idiosyncrasy to the drugs.

Initial Treatment

The period of initial treatment lasted until a conspicuous regression of the subjective and objective signs of thyrotoxicosis showed that the illness was largely under control. Its average duration was twenty-nine days. The dose of thiourea used during this period was 1 g. three times a day; the dose of thiouracil 0·2 g. five times a day. In no case, irrespective of its type, severity, or duration, did the treatment fail to produce conspicuous improvement, and none became drug-resistant. The objective evidence of this is summarized in the table. It will be seen that in every case the pulse-rate and basal metabolic rate (fig. 1) fell while the plasma cholesterol and body-weight rose (Table). The im-

THIOUREA AND THIOURACIL TREATMENT.
INITIAL COURSE OF TREATMENT. RESULTS IN GROUP A (22 PATIENTS).

Dosage	Thiourea 3 g. daily, or thiouracil 1 g. daily.	
Duration of initial course ...	Average 29·3 days.	
Weight change	All gained.	Average 7·7 lb. (range 2 to 15 lb.).
B.M.R.	Fell in all.	Before (average) +39·7 (range +18 to +82).
		After (average) +8·6 (range +30 to −14).
Pulse-rate	Fell in all.	Before (average) 100 day, 87 night.
		After (average) 80 day, 74 night.
Plasma cholesterol	Rose in all.	Before (average) 127 mg./100 ml. (range 83 to 166).
		After (average) 186 mg./100 ml. (range 125 to 310).

provement in symptoms was similarly marked. The sweating, skin flush and nervousness disappeared and diarrhœa, if present, stopped. Two of the cases were fibrillating before treatment was given. One, whose fibrillation was intermittent, became consistently regular; the second, after the pulse-rate had been reduced by thiouracil, was brought back to normal rhythm with quinidine and remained normal. The effect on the eye signs and goitre was less marked. Lid retraction always decreased but exophthalmos was not noticeably altered. In the majority of cases the goitre was unaffected and, in those in which it did decrease, the decrease appeared attributable to diminished vascularity rather than to reduction of glandular tissue. It seems, therefore, that thiouracil and thiourea influence only those symptoms of thyrotoxicosis referable to overfunction of the thyroid gland, affecting slightly, if at all, those symptoms, such as the goitre itself and exophthalmos, which are believed to arise from causes outside the gland.

Thiouracil acts neither immediately nor uniformly upon the symptoms and signs of thyrotoxicosis. The delay before its action varies in different patients. Usually little change is seen in the first and second weeks of treatment, but by the third it is evident
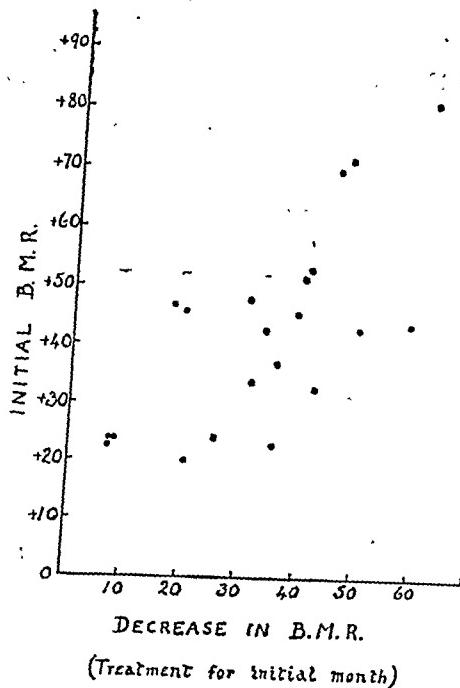
FIG. 1.—Showing that the fall in the basal metabolic rate during the initial course of treatment with thiouracil is roughly proportional to the height of the basal metabolic rate before treatment.

and by the fourth established (fig. 2). In some patients, however, a good response occurs within a few days (fig. 2); in others the response is slow and takes six, eight or more weeks to become established. This latter delayed reaction occurs particularly in patients who, immediately before, have been treated with iodine (fig. 2), and in such cases it is advisable to withhold iodine for one or two months before beginning treatment with thiouracil.

When the treatment begins to take effect the individual symptoms are not all affected proportionately and at the same time. Usually the skin flush disappears early and the raised pulse-rate persists longest. Sweating, nervousness, raised metabolic rate, emaciation and low plasma cholesterol begin to yield at intermediate times, and, generally speaking, in that order. Failure to recognize this sequence in effects has led to certain slow-reacting cases being classified as thiouracil-resistant. Three such cases have been referred to me. In each the subjective improvement, falling basal metabolic rate, and rising weight curve showed that the thyrotoxicosis was being brought under control. The contrary impression was derived from the continued elevation of the pulse-rate; and, with further treatment, this returned slowly to normal levels.

There thus appears to be no question that by means of thiouracil, or thiourea, thyrotoxicosis can rapidly and effectively be brought under control, and that the results of the initial treatment with these drugs are comparable to those achieved by surgery.
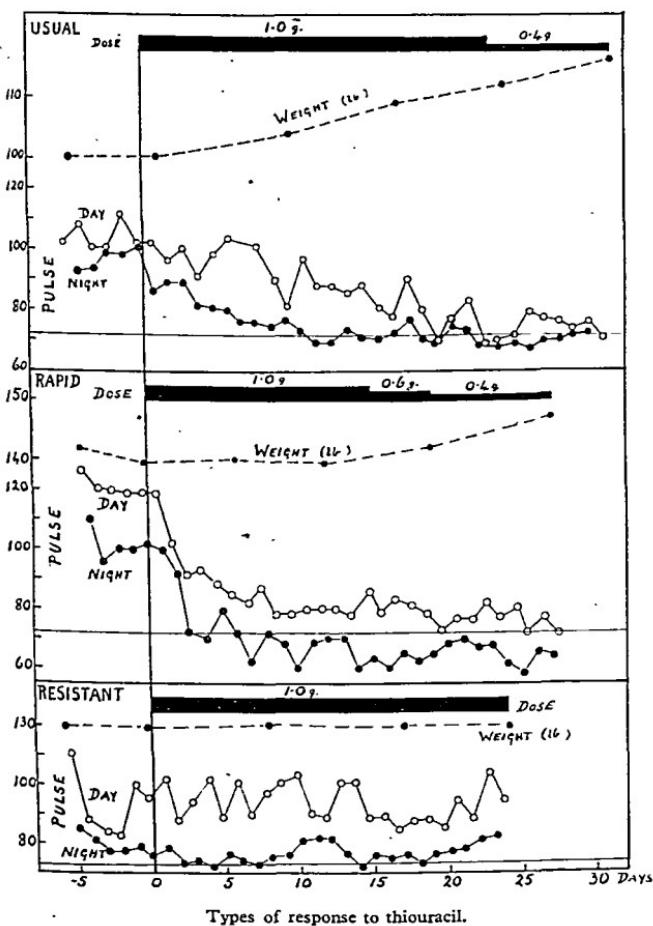
FIG. 2.—Showing differences in the rate of response to thiouracil. The resistant case had received iodine daily for two years before admission, but after a further fortnight's treatment responded. The second case was under the care of Dr. Kenneth Harris.

Types of response to thiouracil.

Maintenance Treatment

It was early realized (Astwood, 1943) that, after the initial course, thiouracil treatment must be maintained at least for some time. But it became evident that far smaller doses were required for maintenance treatment than to establish control, and that it was important to allow for this if symptoms of overdosage were to be avoided. This decrease in requirements is most striking in the early stages; but it extends beyond a simple initial readjustment of dosage and there are indications that it may be progressive. Figs. 3 and 4 illustrate this point. Fig. 3 shows that smaller and smaller doses are required to hold the basal metabolic rate at normal levels and yet the increase in weight is maintained. Fig. 4 shows that doses of thiouracil which at first simply suffice to hold the plasma cholesterol at normal levels later prove too much so that the plasma cholesterol rises suddenly and symptoms of overdosage appear. On the basis of such observations we have been reducing the maintenance dosage more and more rapidly. Most of our patients are now taking 0·1 g. or 0·05 g. daily and in no case has a return of symptoms or a fall in weight suggested that the reduction has been too rapid or too much. This consideration is of particular importance in view of the dangers due to overdosage with the drug.

It would appear that a mechanism exists in the body which resists attempts to force the metabolism below normal. If this were not so then treatment should always produce a steady decrease of metabolism. This does not usually occur in man. As the basal metabolic rate approaches normal its fall slows, even though the dose of thiouracil remains unchanged. Having reached normal, there it tends to remain and its persistence at this level despite subsequent lightening of dosage, suggests that further depression of metabolism is being resisted. The practical importance of this consideration is that evidence of subnormal metabolism should not be awaited before reducing the dose of thiouracil. The dose should be decreased rapidly and continuously until there is
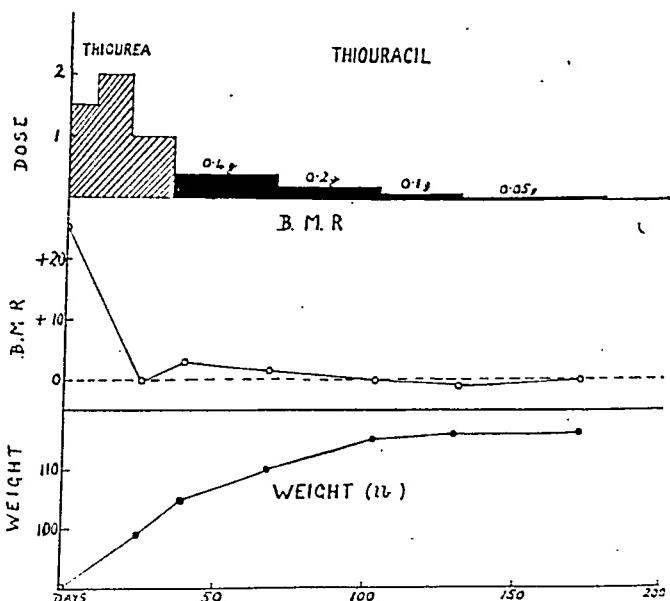
FIG. 3.—Showing that progressively less thiouracil is required to maintain the basal metabolic rate at normal levels.
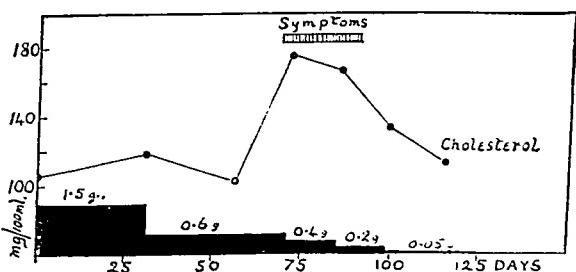
FIG. 4.—Showing the rise of plasma cholesterol, and the associated symptoms of overdosage, which occur when the maintenance dose of thiouracil is not decreased at a sufficiently rapid rate.

evidence that it is insufficient. Then the dose is adjusted appropriately and retained at that level for a few weeks when a further attempt at reduction is made.

The success of any therapeutic method must ultimately be judged by the efficiency with which it restores the patient to normal. In this respect, for periods up to ten months, thiouracil compares favourably with other methods of treating thyrotoxicosis. The majority of patients feel fit to resume full work in one to three months after completion of the initial treatment and, having started, are able to continue. The severity and responsibility of the work offer no bar. One patient is doing full duty as a London

bus driver, another occupying a responsible managerial position, many are looking after their families unaided, and several have returned to industrial work. The disabling symptoms of Graves' disease are thus effectively controlled; but there are two signs which do not appear to be altered significantly even by prolonged treatment. These are exophthalmos and goitre. In two cases, not in my own series, the goitre had eventually to be removed because of pressure symptoms.

It is as yet too early to form an opinion whether treatment with thiouracil can ultimately be discontinued and the patient remain well. Undoubtedly omission of treatment in the early stages is followed by a return of symptoms, but there are hints that later such may not be the result. One of my patients after treatment with thiourea for seventy days, discontinued the drug and has had no treatment for five months. There has been no return of symptoms and she has maintained her weight. Two others have been off treatment with thiouracil for five and seven weeks respectively without showing any untoward effects. None of these cases was severe and before omission of treatment all had been weaned on to very small doses of the drug. It remains to be seen whether their present freedom from thyrotoxic symptoms will be maintained and whether or not this favourable result is unusual.

Overdosage

If thiouracil and thiourea had no untoward effects it would now be reasonably certain that an efficient medical treatment of thyrotoxicosis had been devised. Unfortunately they have such effects and only experience can show whether these occur so frequently as to render treatment with these drugs more dangerous than surgical removal of the gland. In considering their ill-effects it is important to distinguish the effects due to overdosage from those due to idiosyncrasy. By the manifestations of overdosage are meant those symptoms which can be induced in any patient by excessive doses of the drug. By the manifestations of idiosyncrasy are meant those conditions which occur capriciously and inconstantly in a minority of patients.

The manifestations of overdosage can be divided into two groups: The first, which is easily recognized and avoided, occurs early in treatment and from gross overdosage. The second develops insidiously and then quickly becomes manifest, and apparently results from chronic, slight overdosage. Gross overdosage shows itself by an increase in size, sometimes painful, of the goitre. Our first case was discharged from hospital on 2 g. of thiourea daily. He then wore a 15½ in. collar. Within the next two months his neck increased in size so that a 17 in. collar was too small. On reducing the dose to 0·5 g. daily the neck slowly decreased to its original size. A second mild case, who had previously undergone a subtotal thyroidectomy, developed painful nodules all along the operation scar. A third case with a retrosternal goitre developed pressure symptoms. Since adopting a more rapid reduction of dosage after the initial course of treatment few cases of this kind have been seen, and on further reduction of the dose these have all been rapidly relieved.

Chronic, slight overdosage shows itself mainly by subjective symptoms. A patient who for weeks or months has been on the same small dose of thiouracil, and who has previously continued to remark on her improved well-being, comes up complaining of weariness and depression. Not infrequently such cases have a bloated appearance and their friends remark on their lack of energy. Superficially the evidence suggests hypothyroidism but inspection of the weight chart usually shows that the weight has been constant for weeks and determination of the basal metabolic rate shows no depression. This state is associated with, and often preceded by, an elevation of the plasma cholesterol (fig. 4). On reducing the dose the symptoms rapidly disappear and the plasma cholesterol falls. In passing it should be noted that these symptoms are not associated with alteration in the white blood cell count. There is insufficient evidence available at present to decide on the pathogenesis of these symptoms. Are they indeed the first signs of rapidly developing hypothyroidism or are they the results of a toxic action of the drug? The former explanation appears the more probable. But whatever the explanation this type of overdosage is particularly prone to develop during maintenance treatment and can be avoided by reducing the dose to the minimum required to maintain the weight. As a further check the blood cholesterol level can be determined periodically and, if this is rising unduly, the dose of thiouracil should be reduced.

Idiosyncrasy

Fever, rashes, enlargement of lymph glands and blood changes have been reported as manifestations of sensitivity to thiouracil (Astwood, 1943; Gabrilove and Kert, 1944;

Newcombe and Deane, 1944). Fever occurred in 3 of the 33 cases. In 2 it could be accounted for by a coincident infection, one patient having a streptococcal infection of the throat, the other an active infection by *B. coli* of the urinary tract. In both cases the temperature subsided with the infection and did not rise when thiouracil was again given. In the third case no infective cause was found. The fever occurred after the patient had been taking 1 g. of thiouracil daily for eight days and as, unlike the other two, it was associated with a neutropenia the drug was discontinued. The temperature then fell. One patient showed a maculopapular rash on the fifteenth day of therapy with 1 g. of thiouracil daily. As it was unassociated with either fever or leucopenia the drug was continued, though at the reduced dose of 0·4 g. daily; and the rash faded during the next three days. Enlargement of lymph glands has not been observed in our series.

These three manifestations of sensitivity resemble those occurring after many other drugs, not only in their nature but in the delay before their appearance. All have been reported as occurring within a fortnight or so of exposure to the drug and they have not been observed after this time even in cases which have been under treatment for many months. Their appearance early in treatment may be due to the heavy doses of the drug used in the first fortnight, but that this is not the most important factor in their production is evident from the fact that the majority of patients take such doses with impunity. A special sensitivity to the drug is presumably present in the persons affected. In that case the failure of these particular ill-effects to appear after the first fortnight suggests either that the sensitive subjects are few in number and eliminated by early detection, or that desensitization is effected by continued treatment.

The most serious manifestations of sensitivity are those which affect the formed elements of the blood. Leucopenia, agranulocytosis (Astwood, 1943) and thrombocytopenia (Newcombe and Deane, 1944) have been reported. The latter has not occurred in our series but there have been two cases of leucopenia and one case of agranulocytosis out of the 33 cases. The first case of leucopenia was the above patient with the unexplained temperature. At the beginning of the febrile attack the white blood cell count had fallen from 7,800 with 84% of neutrophils to 2,000. At the height of the fever it was 4,400 with 35% neutrophils. The second case received 1 g. of thiouracil daily for fourteen days when a routine blood-count showed 1,100 white cells with 50% neutrophils. Treatment was discontinued and the blood-count rose. This patient had no untoward symptoms throughout. The third case had, on admission, a white count of 10,000 with 68% neutrophils. After treatment for one month with 1 g. of thiouracil daily no improvement in the thyrotoxicosis had occurred. This was attributed to her having received iodine daily for two years before admission. As there had been no toxic symptoms and the white cell count was 9,300 the dose of thiouracil was raised to 2 g. daily. At the end of a further fortnight the thyrotoxicosis had responded, the white cell count was 6,000 with 60% of neutrophils, and the patient was discharged on 0·6 g. daily. Eight days after discharge she developed a whitlow, two days later she felt chilled, the temperature rose to 104°F. and two days after she developed a sore throat. On admission she had 1,500 white cells with no neutrophils and only a few primitive cells were present in the sternal marrow. Vigorous treatment with fresh blood transfusions and pentnucleotide was given. Neutrophils returned to the blood four days later. Six days after admission the white count was 26,000 with 76% of neutrophils and the sternal marrow showed vigorous activity and mature cells. Then, unfortunately, she contracted a bronchopneumonia and from this she died.

Agranulocytosis being the most dangerous complication of treatment with thiouracil or thiourea it is important to consider the factors concerned in its production. It is evident that idiosyncrasy plays a part. If an invariable action of these drugs were to depress the production of neutrophils then it would be expected that these would fall in all patients. This does not happen. In the series of 22 patients shown in the table the white cell counts on admission ranged from 4,000 to 10,000 with an average of 6,513; the neutrophils ranged from 42% to 80% with an average of 59·3%. On the completion of the initial treatment the white counts ranged from 3,000 to 11,600 and averaged 6,865; the neutrophils ranged from 40% to 81% and averaged 59·6%. Throughout the period of maintenance treatment white cell counts have been done on all patients at intervals of not more than one month. Again there is no evidence of a consistent and steady depression of neutrophils as treatment continues. Neutropenia, when it occurs, appears suddenly in patients whose previous blood-counts have been normal both in respect of total white cells and total neutrophils. There is a hint, however, that its supervention may be foreshadowed by the appearance of many young neutrophils in the peripheral

blood.   This possibility is being investigated.   Lastly, neutropenia does not develop until a week or more after treatment has commenced, an observation which may be explained either by a cumulative toxic effect or a developing sensitivity.   Despite this evidence of idiosyncrasy, there is, however, an indication that the development of neutropenia is also influenced by the dose of thiouracil used; not by the total dose given over many months but by the intensity of the daily dosage.   The three cases reported here all occurred either during or shortly after intensive treatment.   Astwood's fatal case was receiving 2 g. of thiouracil daily; Newcombe and Deane's case of thrombocytopenia and leucopenia had taken 83 g. of thiourea in five weeks; and a third fatal case, of which I have been informed, had received 103 g. of thiourea and 62 g. of thiouracil in five months. As far as I am aware no cases have been reported of any manifestations of sensitivity in patients taking thiouracil in small doses of the order of 0·1 or 0·05 g. a day.

It thus appears that two factors are involved in the production of this untoward effect of thiouracil: idiosyncrasy and dosage.   If this be so then we may hope to avoid it by using small doses of the drug.   For this reason, and because of the evidence that the maintenance doses have been greater than necessary, it seems advisable to use, in all stages of the treatment, smaller doses of thiouracil than have been used up to now.   The dosage which is being tested at present is 0·5 g. daily until the B.M.R. falls to about +10%. Thereafter the dose is decreased to 0·1 g. or 0·05 g. daily during the maintenance period. It is hoped, on the basis of analogy with the sulphonamide drugs, that by using these smaller doses and reducing the dose more rapidly a safe yet effective technique of this promising therapy may be evolved.   For the present, however it, should be realized that thiouracil therapy is still in the experimental stage and that it should only be used under circumstances which allow close, detailed and continued investigation of the patients.

REFERENCES

ASTWOOD, E. B. (1943) *J. Amer. med. Ass.*, **122**, 78.
GABRILOVE, J. L., and KERT, M. J. (1944) *J. Amer. med. Ass.*, **124**, 504.
HIMSWORTH, H. P. (1943) *Lancet* (ii), 465.
NEWCOMBE, P. B., and DEANE, E. W. (1944) *Lancet* (i), 179.
WILLIAMS, R. H., and BISSELL, G. W. (1943) *New Engl. J. Med.*, **229**, 97.

Mr. C. A. Joll (*in absentia*): There have been so many calls from practitioners and others to be supplied with thiouracil and thiourea for the treatment of their patients that it seems desirable to give a preliminary report of the results we have been getting, both good and bad, if only to make it clear to those who wish to make use of these powerful and dangerous drugs that some of the optimistic statements which have been made in this country—be it emphasized, often on a very slender experience—are at any rate extremely ill-judged.

Thyrotoxicosis is a name which embraces a group of diseases, among which the form which we call primary thyrotoxicosis or Graves' disease is perhaps best understood.   It is also the easiest form to diagnose and, in some ways, to treat, and it is associated with a hyperplastic thyroid gland which, in spite of infinite variations in detailed histology, conforms more or less closely to type.   I was glad to note that this Section has used the term "thyrotoxicosis" and not begged the question of the nature of the disease by using the unjustifiable term *hyperthyroidism*, since we do not even know the exact nature of the normal thyroid hormone, much less the chemistry of the abnormal products associated with thyrotoxicosis.

So far, all or nearly all the work on thiouracil and thiourea has been in connexion with this variety of thyrotoxicosis and little or nothing has emerged in relation to the much larger, more insidious and more hazardous groups of cases we include under "secondary thyrotoxicosis".   The pathology of this "secondary" type is the reverse of uniform and in fact thyrotoxic symptoms may be met with in nearly every variety of pathological thyroid gland, but on the whole one may say that in this vast and inchoate group *hyperplastic changes* are either entirely absent or at any rate inconspicuous in degree or trivial in extent.   It is hardly to be expected that the hyperinvoluted thyroid gland met with so often in these circumstances is as likely to respond to substances such as thiouracil and thiourea by increased hyperplasia as do the forms in which diffuse hyperplasia already exists.   It is probably wise until our information is more complete in connexion with the relatively simpler problem of primary thyrotoxicosis, not to confuse the issue by exhibiting thiouracil in the secondary forms of thyrotoxicosis.

Wartime conditions have limited the number of cases we have been able to observe to between 20 and 30, and of these I have taken only 9 cases which are fully documented to illustrate our results.   Group I: 6 cases showing favourable results.   Group II: 3 cases showing unfavourable results.

Group I.—Favourable cases: In this group 3 cases should be regarded as very mild in degree, one of moderate severity and two severe.

CASE I.—K. S., female, aged 42. A classical severe case with a ten-months' history of nervousness, trembling and palpitations. Loss of weight 2 st. in ten months. The B.M.R. was + 49% and the heart overacting. Thiouracil 0·6 g. daily for twenty days was given followed by a maintenance dose of 0·2 g. as an out-patient for five weeks. In fifty days she had put on 1 st. in weight and felt better, although her B.M.R. did not fall and her pulse-rate remained about 100.

(a)   (b)   (c)

CASE I.—K. S. Showing condition (a) before thiouracil treatment, (b) after two months' treatment, (c) after ceasing to persevere with maintenance dose.

She has failed to go on with her maintenance dose of thiouracil and her condition has deteriorated rapidly although there is a slight gain in weight. Her heart is severely overactive and her pulse-rate has risen to 150. She refuses operation—and a significant fall in polymorphonuclear leucocytes over four months after cessation of the drug makes future treatment difficult.

CASE II.—B. L., female, aged 52. A case of moderate severity with four years' history of fatigue, tremor and palpitations. A small hyperplastic goitre was palpable. She had obvious exophthalmia. Her B.M.R. was + 46%. Thiouracil 0·6 g. daily for three weeks was given followed by 0·2 g. daily maintained as an out-patient. In ten weeks
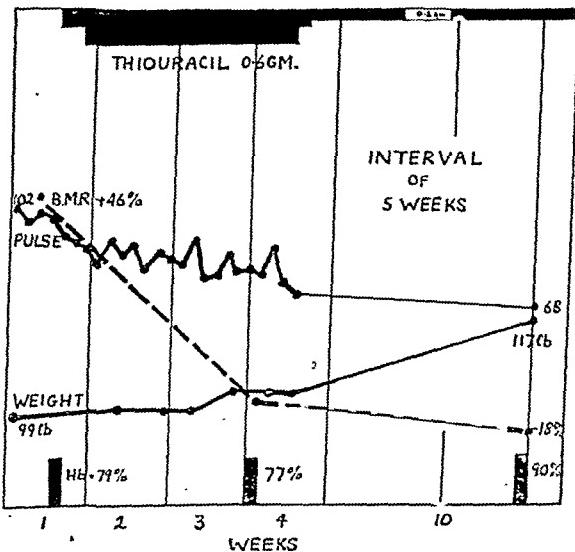
CASE II.—B. L. Illustrating favourable effect of thiouracil.

her pulse fell from 102 to 68 and she put on 18 lb. in weight. Her B.M.R. fell to − 18%. The only adverse effect noted was muscle cramps.

CASE III.—M. T., female, aged 45. A mild case with a history of six months' lassitude, tremor and palpitations. There was no classical exophthalmos but Dalrymple's sign was positive. The B.M.R. was +25%. Thiouracil 1·2 g. daily for three days was given,

then 0·6 g. daily for nineteen days, followed by 0·2 g. maintenance dose. Her subjective symptoms improved, her B.M.R. fell to −14% and her weight rose 12 lb. during her

(a) (b) (c)

CASE III.—M. T. Showing condition (a) before thiouracil treatment, (b) after two months' treatment, (c) after seven months' treatment.

in-patient treatment. As an out-patient the B.M.R. rose to normal, the pulse to 90, but she continued to feel well and to put on weight.

CASE IV.—J. T., female, aged 19. A mild case with a history of palpitations of only three months' duration. There had been no loss of weight. The pulse-rate was abnormally high (140) but the B.M.R. only +21%. Thiouracil 0·6 g. daily for three weeks was given, then 0·2 g. daily as an out-patient. Over a period of six months she has put on 1 st. in weight and her B.M.R. has fallen to −29%. The effect on the pulse has never been quite as marked, it is still 100—a disadvantage, since this was her presenting symptom. She developed purpura under treatment and the drug has therefore been stopped temporarily.

CASE V.—L. V., male, aged 38. A severe case with a history of increasing fatigue, prominence of eyes, dyspnœa, and tremor and of loss of 3 st. in weight in three months.
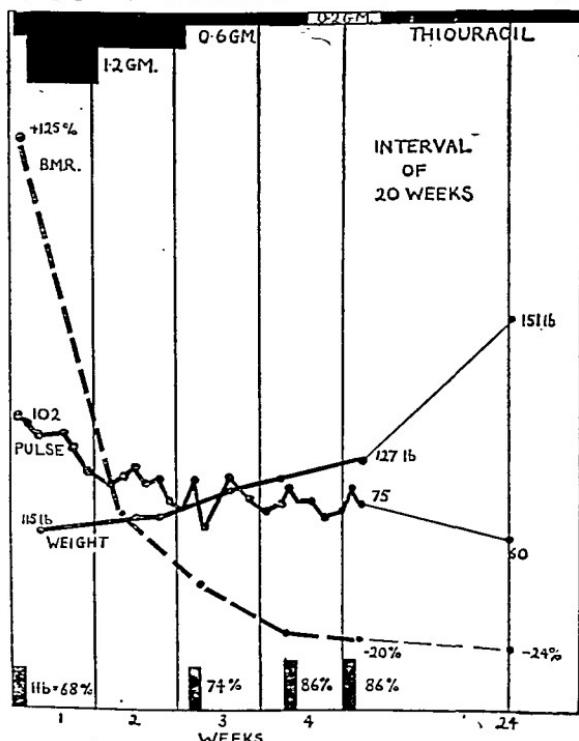
CASE V.—L. V. Illustrating favourable effect of thiouracil in a severe case.

Previous treatment had included *two courses of deep X-ray therapy at another hospital*, in addition to iodine therapy and psychological treatment. The B.M.R. rose from +16% to +44% during treatment and on admission to us the B.M.R. was estimated at +125%. Thiouracil 1·2 g. daily for one week was given, then 0·6 g. daily for one week followed by 0·2 g. daily for two weeks maintained as an out-patient.

His clinical condition improved in every respect during in-patient treatment, the pulse fell from 102 to 75, he put on 12 lb. in weight and the B.M.R. fell to −20%. After five months on the maintenance dose of 0·2 g. his pulse is 60, his weight has gone up a further 24 lb. and the B.M.R. is −24%. There has been a slight tendency to a fall in his white blood-count but this is not apparently progressive.

CASE VI.—D. S., female, aged 38. A mild case, with five weeks' history of nervousness, palpitations and sweating. There was no exophthalmos. The pulse was 130 and the B.M.R. +32%. A typical hyperplastic goitre was palpable. Thiouracil 1·2 g. daily for one week was given, then 0·6 g. daily for one week followed by 0·2 g. daily for one week.

There was a definite improvement in all the physical signs including a fall in pulse-rate and in B.M.R. to −12%. The patient said, however, that she felt no better and requested operation, which was carried out. Sixteen weeks later her B.M.R. is −40% and her weight has risen from 7 st. 8¼ lb. to 8 st. 10 lb. (This is a case which should not be regarded as a thiouracil failure, but rather one in which its effect was purely physical, while the patient's symptoms were markedly psychical.)

Group II.—Unfavourable cases.

CASE VII.—D. R., female, aged 41. A moderately severe case with a history of loss of 3 st. in weight, palpitations and dyspnœa for a year and a half. She had had iodine therapy ℳ xx t.d.s. for only two weeks before admission. Her B.M.R. was +65%. Thiouracil 1·2 g. daily for seven days was given, then 0·6 g. daily for seven days, followed by 0·2 g. daily for six days.

Under this regime the B.M.R. fell slightly to +54%, but her weight fell a further 5 lb. and the pulse was unaffected. The patient chose operative treatment rather than the risk of further deterioration. After operation the B.M.R. fell to +6%, her weight rose and pulse fell rapidly.

CASE VIII.—E. B., female, aged 39. A severe case with a history of at least two years' duration, with loss of weight, palpitations and nervousness. She had had prolonged iodine therapy elsewhere. Her pulse was 130 and her B.M.R. +67%. Thiouracil 0·6 g. daily for one week was given followed by 0·4 g. daily for two weeks.

There was very little fall in pulse-rate or B.M.R. and the patient asked for operation, since she felt no better. Eighteen days after the operation the B.M.R. had fallen to −4%, the pulse to 70 and weight had begun to rise.

CASE IX.—L. S., female, aged 36. A moderate case with a classical history of fatigue, palpitations, loss of weight, &c. She had had four months' iodine therapy. The B.M.R. was +43% and the heart severely overacting. Thiouracil 0·6 g. daily was given. After three weeks there was a sudden fall in blood granulocytes (absolute polymorph. count of 31) with ulceration of fauces and pyrexia to 102° F. No improvement in the blood-count followed discontinuance of thiouracil until six days later, when gradual improvement was noted after a fresh blood transfusion. The B.M.R. rose to +53% six weeks after starting treatment, the pulse-rate was not improved and a further fall of body-weight was noted.

Thyroidectomy two months after admission resulted in a fall of B.M.R. to −19% and of pulse-rate to 80.

To sum up this brief series, it would be fair to include Case VI in the number which I have stated to be so far favourable, since no adverse thiouracil effect was noticed and the patient's lack of co-operation was the main obstacle to success.

If this be conceded, then two-thirds of the cases responded well to thiouracil and one-third unfavourably. This is, however, very far from claiming that similar figures could be obtained over a really large series and it leaves quite untouched the great mass of thyrotoxic cases which are not in the "primary" category. I very much hope that this line of treatment will be followed up under strict control and that the manufacturing chemists will not release these powerful and dangerous drugs to all and sundry. Much work still remains to be carried out, I submit, in connexion with the value of thiouracil, not necessarily as a method of treatment *sui generis* but in relation to the possibility of using it instead of iodine therapy as a means of preparation for operation. If the optimum reduction in thyrotoxicosis could be rapidly obtained (as seems possible) so that operative risks could be ignored, then an epoch-making step will have been made in the therapeusis of thyrotoxicosis.

Dr. Horace Evans: I have had the opportunity of treating twelve thyrotoxic patients with thiouracil, eight of these under careful control at the London Hospital. In every instance the result was very satisfactory, closely agreeing with Himsworth's cases. The exophthalmos, with one exception, was not improved. No ill-effects of the drug occurred, but in one patient a transient neutropenia was observed. In a critical review of these cases it must be remembered that even in the best hands the results of surgical treatment are by no means always good. It is of course too early to judge final results of thiouracil therapy but I feel that the initial treatment is satisfactory. This treatment is still in the experimental stage and the use of this drug, except under careful control, is to be deprecated.

Dr. G. Melton: The following case illustrates the influence of thiouracil on auricular fibrillation complicating thyrotoxicosis.

L. H., female, aged 63. Admitted 2.10.43.

History.—Goitre five years. For past three months dyspnœa, nerviness, tremor, diarrhœa, loss of weight, cough, sweating and swollen legs. Remained up and about.

On examination.—Orthopnœa; cyanosis; thin; nervy; sweating and tremor of hands; exophthalmos, goitre involving left side and isthmus. Cervical veins engorged. Œdema of legs and sacrum. Lung bases congested, particularly right. Heart: Apex beat 5th left interspace 1½ in. outside M.C.L., grossly irregular, rate 116 per minute, systolic murmur apex. B.P. 190/90 (approx.). Abdomen—liver enlarged with ascites. Urine normal. Optic fundi: Narrowing of arteries. Electrocardiogram: Auricular fibrillation; left axis deviation. Basal metabolic rate (6.10.43) +80%.

Progress.—Following digitalization and mersalyl injections there was marked improvement in the signs of congestive failure. 25.10.43: Heart: Rate 80-90. Still auricular fibrillation. B.P. 215/110. B.M.R. +38%. 1.11.43: Thiouracil commenced 0·6 g. daily. 18.11.43: Cardiac rhythm now regular, rate 70-80. E.C.G. normal rhythm. 21.11.43: B.M.R. +28%. 14.12.43: Commenced to get up and later developed slight tachycardia 80-90 per minute. 28.1.44: Thiouracil discontinued. No granulocytopenia or thrombocytopenia. 14.2.44: B.M.R. +17%. Has gained 22 lb. in weight. Has remained well since, continuing to put on weight. No recurrence of congestive failure, auricular fibrillation or thyrotoxicosis. On digitalis foliata 2 gr. daily. Maximum urea clearance 40% normal. Goitre and exophthalmos I.S.Q. Hypertension persists.

Comment.—Despite initial improvement with rest and digitalization, thyrotoxic signs and auricular fibrillation persist. Following thiouracil, cardiac rhythm became normal, B.M.R. continued to fall, weight to increase and other thyrotoxic signs and symptoms cleared up, apart from the goitre and exophthalmos. Since discontinuing thiouracil her condition has remained satisfactory for six months. She also has essential hypertension, which was a probable factor in the production of her congestive failure, particularly in view of the striking improvement which followed rest and digitalization.

Dr. S. L. Simpson said that although the interpretations of the data presented by Professor Himsworth and Mr. Joll apparently differed in some respects, there was a large measure of agreement in the objective data presented. There was no doubt that, in a good proportion of patients with thyrotoxicosis, thiouracil produced a significant and often dramatic fall in pulse-rate and basal metabolic rate, and an increase in weight. The increase in weight was sometimes disproportionately great and might be due, in addition to the decreased metabolic rate, to the changes produced in the pituitary gland, namely, hypertrophy, hyperplasia, and vacuolization of the basophil cells. Further investigation would determine which types of thyrotoxicosis were refractory to thiouracil, but there did not appear to be sufficient evidence in support of the statement that secondary thyrotoxicosis (toxic adenoma) was refractory. That thiouracil did not abolish exophthalmos was not surprising, since thyroidectomy often failed to influence exophthalmos, a condition which could be produced by the pituitary thyrotrophic hormone in the absence of the thyroid gland. Both thiouracil and thyroidectomy, however, diminished, or abolished, pathological lid retraction, and the associated characteristic staring expression of thyrotoxic patients.

Thiouracil acted by inhibiting the synthesis of thyroxine, to which the organism responded by an increased secretion of the pituitary thyrotrophic hormone, and resulting increased hyperplasia of the thyroid gland. It therefore was only to be expected that the thyroid gland would not diminish in size and might increase in size. Therefore, thiouracil should not be used in patients where pressure symptoms were already a feature, or where a grossly enlarged thyroid gland was unacceptable for æsthetic or psychological

reasons. The tadpole was the only experimental animal where thiouracil produced an atrophy of the thyroid rather than a hyperplasia. It might be that hyperplasia in man would, after some time, give way to exhaustion atrophy, perhaps with myxœdema, as sometimes happened spontaneously.

Both thiouracil and thiourea were dangerous drugs, and in addition to the reactions recorded by others, Dr. Simpson stated that in one of his patients in whom thiourea produced a fall in basal metabolic rate from $+46\%$ to -20%, delusional insanity developed. This might occur spontaneously in both thyrotoxicosis and myxœdema, but its onset within a few weeks of starting the drug could not be ignored. Nevertheless, thiouracil, or a modified substance, without its toxic reactions, would probably find an important place in medical therapeutics. At present it should only be used with caution and under controlled conditions.

Professor Himsworth, in reply, said that in his experience thiouracil had worked effectively in all types of thyrotoxicosis. The three cases reported by Mr. Joll in which its action had been slight or absent could adequately be accounted for by the fact that all three had received iodine up to the time of commencing thiouracil treatment and that after such premedication little effect from thiouracil would be seen in the short periods of treatment of three and four weeks which these cases received.

Proceedings of the Royal Society of Medicine

Section of Physical Medicine

President—P. BAUWENS, M.R.C.S., L.R.C.P.

[February 16, 1944]

The Relation of Physiotherapy to Plastic Surgery

By J. P. REIDY, F.R.C.S.

THE practice of plastic surgery neither begins nor ends with the remodelling of features or the transference of tissue from one area to another. During the stages of treatment by plastic surgery the demands on physiotherapy are many and varied, and no field of surgery presents so many problems or demands such close co-operation from physiotherapists in achieving results. It is desirable, therefore, that a staff member of the Physiotherapy Department should be included in the plastic surgery team in hospital, to attend on all rounds and to contribute to the discussion on patients from that aspect.

It is my intention to give a brief survey of some of the plastic surgery undertaken at Ministry of Pensions Hospital, Stoke Mandeville, under the direction of Professor T. P. Kilner, and to indicate how much we call on the physiotherapists under the direction of Dr. Francis Bach.

I will refer chiefly to various types of skin grafts, burns and limb conditions. (Here slides were shown illustrating the different types of skin grafts and reference was made to phase of contraction, pigmentation, and suitability of each type of graft.)

Ideally, the physiotherapists are asked to co-operate under these headings:

(1) *Preoperative application.*—General: Breathing exercises to reduce anæsthetic problems, e.g. in old people. Local: (*a*) Heat and massage to improve movements and circulation—in limbs about to be immobilized; in areas about to be excised, or grafted; and to soften and loosen scars prior to excision. (*b*) Burns of hands. The immediate treatment favoured is that of the Bunyan bag and irrigation with Milton (1-5%). The advantages of the Bunyan bag are relief of pain; provision of a transparent occlusive dressing; ease of nursing; a method of preventing infection and clearing infection already present. Splinting can be applied outside the bag or movements and exercises encouraged in the bag.

(2) *Intermediate application.*—(*a*) Improving circulation of, say, an abdominal tubed pedicle, before transference. (*b*) Heat and massage to cramped upper and lower limbs during intermediate stages of operations, chiefly concerned during the transference of a tubed pedicle to distant areas.

(3) *Postoperative application.*—Indirect: Restoration of movements and circulation in cramped shoulders, forearms, &c., when fixation is removed. Treatment in nerve and muscle lesions. Direct: Treatment to all types of grafts, free and pedicled, to reduce the degree of contracture in free grafts, and to improve circulation and appearance of suture lines in all types. For the free grafts, light rotatory grease massage is usually employed. This is easily taught to the patient who can continue it out of hospital.

(4) *Remedial application.*—(*a*) Purposive splinting with exercises against elastic resistance to increase range and power of movement, e.g. in burned hands. (*b*) Active exercises designed to restore movement, e.g. jaw exercises after bilateral condylectomy; restoration of function in stiff limbs following fixation in hand joints after burns and/or skin grafting. These exercises are accompanied by massage, heat, saline soaks, and wax baths; galvanism when required.

Exercises are graded into—Light: string bag making, basketry, chair-seat making, light carpentry. Heavy: rowing, bicycling, foot-operated loom, and treadle-saw, exercises against weights, walking and games.

(Photos were shown giving examples under each section.)

Particular stress was laid on certain problems: (1) Contractures of scars and grafts. (2) Maintenance of function during fixation of limbs and of recently burned hands. For the latter it is claimed that Bunyan bag treatment fulfils the ideals. (3) Restoration of function in stiff limbs; in burn contractures of hands; in nerve and muscle lesions. (4) How to keep the patient interested in his own progress during long convalescence, e.g. by variation of exercises and games. (*See figs.*)

Summary.—The relation of physiotherapy to plastic surgery was discussed. Various types of skin grafts and flaps were illustrated, demonstrating the need for physiotherapy in different stages.

The problem of contractures in scars, grafts and burned hands was referred to. It was shown that adequate and timely application of physiotherapy will do much to limit the degree of contracture and to soften scar tissue, at the same time improving local circulation. Suppleness and smoothness of grafts can be maintained.

(A film was shown illustrating "Thiersch grafting for ectropion of eyelids", by Professor T. P. Kilner.)

My thanks are due to Professor T. P. Kilner for allowing me to show slides and the film from his personal records and photos of cases treated in the Plastic Unit at Stoke Mandeville.

Dr. Francis Bach stressed the necessity for close co-operation between the physiotherapist and the plastic surgeon. He described the Physical Medicine and Occupational Therapy Departments and the work of the quartermaster-sergeant instructor which were under his charge at the hospital run by the Ministry of Pensions at Stoke Mandeville.

A masseuse was seconded to the Plastic Unit to work closely with the plastic surgeon. She went on the ward rounds, attended operations and was responsible for the more specialized physical treatment of the patients in the Unit. The occupational therapist and the sergeant-instructor also had an important role to play in helping the patient to regain his general fitness as well as improving the function of that part of the body for which the patient was under treatment.

An analysis of 100 consecutive patients referred to the Physical Medicine Department from the Plastic Unit showed :—

Burns to Face	...	...	22	Gunshot wounds	...	...	...	...	...	12
Hands	...	...	18	Ulcers (both traumatic and varicose) ...	...	...	...	...	5
Arms	...	...	4	Infective conditions (such as excision of scar after lupus and after					
Eyes	...	...	3	compound fractures)	...	...	...	...	...	15
Legs	...	...	3	Congenital deformities (such as webbed fingers, cleft palates and					
				nævi)	...	...	...	...	...	10
		Total	50	Dupuytren's contraction and non-plastic conditions	...	...			8

The main methods of physical treatment employed were: *Massage of the skin graft.* Grease and paraffin were used to improve the blood supply, to get the graft supple and to reduce œdema. *Wax baths and short wave* (coil) to improve the circulation and the atrophied skin, especially of the extremities. *General and local light* to improve the general health as well as to treat the local sepsis. *Splinting, manipulation and exercising* of the stiff joints. *Slings and pulleys* for the treatment of weak muscles. (Stronger slings and weights are used when the muscles are stronger.) *Electrical stimulation with faradism* for weak muscles. *Forced movements. Pre- and post-operative exercises* to relieve pain and stiffness due to local fixation of limb to which a pedicle flap is attached. *Remedial and class exercises* under a sergeant-instructor. *Occupational therapy.*—Remedial and diversional work in the wards and in the Department.

In Dr. Bach's opinion further study should be made in order (a) to prevent the transient nerve paralysis which sometimes follows limb immobilization; he referred to two ulnar palsies that had been under his care. (b) To improve the methods used for increasing the peripheral circulation before and after surgical treatment by means of short wave, pavex machine, ultraviolet light, &c.

Dr. Bach also suggested that the physician in charge of the Physical Medicine Department and his technical staff should co-operate closely with the plastic surgeon who is responsible for the planning and the carrying out of the series of operations so necessary in many cases if a successful plastic result is to be obtained.

Dr. F. S. Cooksey: The contribution of physical medicine to plastic surgery falls under two heads: First, the general rehabilitation of the subjects of plastic surgery and, secondly, the use of physical therapy such as massage, electrotherapy, exercises and occupational therapy to assist the restoration of function in the damaged area. In suitable cases these methods should be applied promptly and freely. Under wartime conditions a large proportion of cases are burns causing facial disfigurement or crippling deformity of the hands. Most are long-term cases with many operations interposed between tedious periods of waiting. Many patients are capable of working but the interruption of work for operations and treatment makes them a burden to industry. The ordinary methods of rehabilitation by physical exercises, occupational therapy in the form of handicrafts and recreational activities are inadequate since these long-term and disfigured patients start with low morale and soon become bored. Above all it is essential to persuade them from the earliest moment that they will be able to resume a normal social and industrial life. Ideally they should live at home and work in a suitable office or factory in the intervals between treatment; but when hospitalization is necessary the most satisfactory form of occupational therapy is the provision of a factory in or adjacent to the hospital wherein patients work under industrial discipline for regular hours at the standard wage for the work done. When patients are confined to bed or the disability prevents work under industrial conditions the newly-developed methods of remedial occupational therapy fill a useful role.

In the past most deformities due to scar contraction found their way to the physiotherapy departments; but, more often than otherwise, the response to long periods of treatment was disappointing. To-day the excision of the scar and substitution of a graft leads to the immediate restoration of substantial, if not full, movement to joints which appeared to be intractably stiff. Plastic surgery has made an invaluable contribution to the management of cases which have been the source of endless work and disappointment. New grafts are œdematous until lymphatic circulation is established and massage with olive oil is useful to soften the graft and reduce the œdema. Assisted or active

FIG. 1.—X-ray burns of hand. Excision of scar tissue and Thiersch graft.
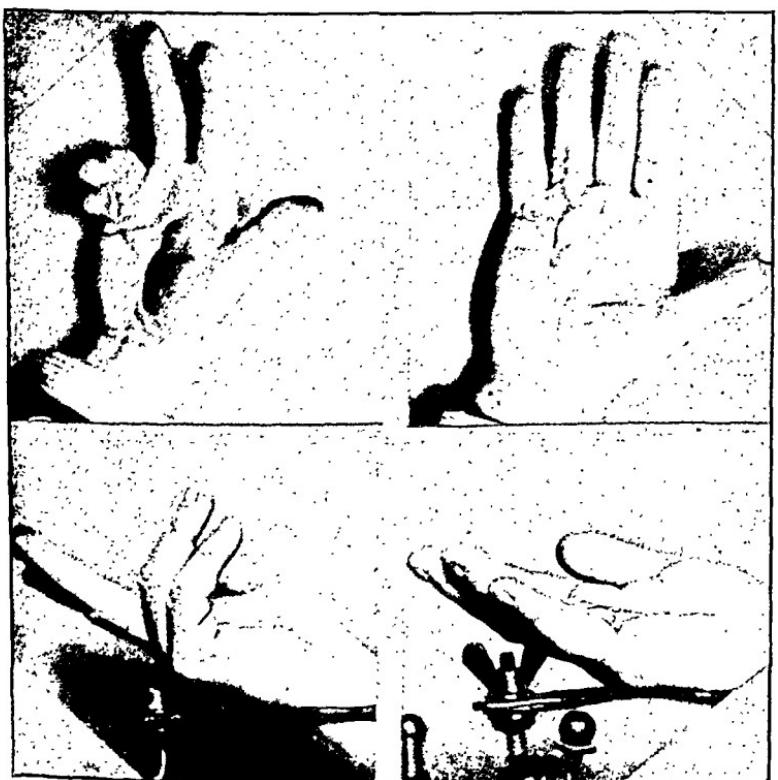
FIG. 2.—A case of Dupuytren's contracture treated by free excision of fibrosed fascia and skin. A Thiersch graft was employed to cover the raw surface which remained.

The problem of contractures in scars, grafts and burned hands was referred to. It was shown that adequate and timely application of physiotherapy will do much to limit the degree of contracture and to soften scar tissue, at the same time improving local circulation. Suppleness and smoothness of grafts can be maintained. (A film was shown illustrating "Thiersch grafting for ectropion of eyelids", by Professor T. P. Kilner.)

My thanks are due to Professor T. P. Kilner for allowing me to show slides and the film from his personal records and photos of cases treated in the Plastic Unit at Stoke Mandeville.

Dr. Francis Bach stressed the necessity for close co-operation between the physiotherapist and the plastic surgeon. He described the Physical Medicine and Occupational Therapy Departments and the work of the quartermaster-sergeant instructor which were under his charge at the hospital run by the Ministry of Pensions at Stoke Mandeville.

A masseuse was seconded to the Plastic Unit to work closely with the plastic surgeon. She went on the ward rounds, attended operations and was responsible for the more specialized physical treatment of the patients in the Unit. The occupational therapist and the sergeant-instructor also had an important role to play in helping the patient to regain his general fitness as well as improving the function of that part of the body for which the patient was under treatment.

An analysis of 100 consecutive patients referred to the Physical Medicine Department from the Plastic Unit showed :—

Burns to Face	...	...	22	Gunshot wounds	...	...	...	...	12
Hands	...	...	18	Ulcers (both traumatic and varicose)	...	...	...	...	5
Arms	...	...	4	Infective conditions (such as excision of scar after lupus and after compound fractures)					15
Eyes	...	...	3						
Legs	...	...	3	Congenital deformities (such as webbed fingers, cleft palates and nævi)					10
	Total		50	Dupuytren's contraction and non-plastic conditions		...	...	...	8

The main methods of physical treatment employed were: *Massage of the skin graft.* Grease and paraffin were used to improve the blood supply, to get the graft supple and to reduce œdema. *Wax baths and short wave (coil)* to improve the circulation and the atrophied skin, especially of the extremities. *General and local light* to improve the general health as well as to treat the local sepsis. *Splinting, manipulation and exercising* of the stiff joints. *Slings and pulleys* for the treatment of weak muscles. (Stronger slings and weights are used when the muscles are stronger.) *Electrical stimulation* with faradism for weak muscles. *Forced movements.* Pre- and post-operative exercises to relieve pain and stiffness due to local fixation of limb to which a pedicle flap is attached. *Remedial and class exercises* under a sergeant-instructor. *Occupational therapy.*—Remedial and diversional work in the wards and in the Department.

In Dr. Bach's opinion further study should be made in order (a) to prevent the transient nerve paralysis which sometimes follows limb immobilization; he referred to two ulnar palsies that had been under his care. (b) To improve the methods used for increasing the peripheral circulation before and after surgical treatment by means of short wave, pavex machine, ultraviolet light, &c.

Dr. Bach also suggested that the physician in charge of the Physical Medicine Department and his technical staff should co-operate closely with the plastic surgeon who is responsible for the planning and the carrying out of the series of operations so necessary in many cases if a successful plastic result is to be obtained.

Dr. F. S. Cooksey : The contribution of physical medicine to plastic surgery falls under two heads: First, the general rehabilitation of the subjects of plastic surgery and, secondly, the use of physical therapy such as massage, electrotherapy, exercises and occupational therapy to assist the restoration of function in the damaged area. In suitable cases these methods should be applied promptly and freely. Under wartime conditions a large proportion of cases are burns causing facial disfigurement or crippling deformity of the hands. Most are long-term cases with many operations interposed between tedious periods of waiting. Many patients are capable of working but the interruption of work for operations and treatment makes them a burden to industry. The ordinary methods of rehabilitation by physical exercises, occupational therapy in the form of handicrafts and recreational activities are inadequate since these long-term and disfigured patients start with low morale and soon become bored. Above all it is essential to persuade them from the earliest moment that they will be able to resume a normal social and industrial life. Ideally they should live at home and work in a suitable office or factory in the intervals between treatment; but when hospitalization is necessary the most satisfactory form of occupational therapy is the provision of a factory in or adjacent to the hospital wherein patients work under industrial discipline for regular hours at the standard wage for the work done. When patients are confined to bed or the disability prevents work under industrial conditions the newly-developed methods of remedial occupational therapy fill a useful role.

In the past most deformities due to scar contraction found their way to the physiotherapy departments; but, more often than otherwise, the response to long periods of treatment was disappointing. To-day the excision of the scar and substitution of a graft leads to the immediate restoration of substantial, if not full, movement to joints which appeared to be intractably stiff. Plastic surgery has made an invaluable contribution to the management of cases which have been the source of endless work and disappointment. New grafts are œdematous until lymphatic circulation is established and massage with olive oil is useful to soften the graft and reduce the œdema. Assisted or active

that. the whole system of light and dark rings is deflected when the beam of electrons emerging from the gold leaf on its way to the photographic plate is passed through a strong magnetic field. Such a magnetic field would have no effect on light waves or X-rays.

The fundamental theoretical investigations of L. de Broglie in 1925 and the experimental researches of G. P. Thomson in 1928 established the existence of a wavelength of the electron which was found to be extremely short in comparison with the wavelength of light. The electron wavelength measured in cm. is

$$\lambda = \frac{1 \cdot 22.10^{-7}}{\sqrt{V}} \times \frac{1}{\sqrt{(1 + 10^{-6}V)}}$$

λ depends only upon the electron energy V, which, in the equation is measured in ev.

Electron rays of 20 to 100 kv. energy can easily be produced by electrical discharges in gases or by an acceleration of electrons emitted from a hot cathode. A stream of electrons can easily be given velocities up to 100,000 miles a second by the influence of high voltages. With an accelerating voltage of about 60,000, which is commonly used in the high voltage cathode-ray oscillograph, the velocity attained is about 150,000 km. per second (about half that of light), and the associated electron wavelength is then about 100,000 times smaller than the wavelength of visible light. If such a beam of electrons could be used as light rays are in the microscope, one would expect a corresponding increase in magnifying and resolving power One red blood corpuscle would be enlarged to seven metres. This does not work out in practice, as there are physical limitations, which greatly reduce the useful magnification obtainable.

ELECTRON OPTICS

A beam of electrons is a stream of negatively charged particles and can be bent by means of magnetic or electrostatic fields to bring them to a focus. A procedure of this kind is followed in the electron microscope. The optics of electron rays are in some ways comparable to those of light rays, but instead of using glass lenses, the focusing agents are electric or magnetic fields (*see* fig. 1). The bending does not take place suddenly as in glass lenses, but gradually.
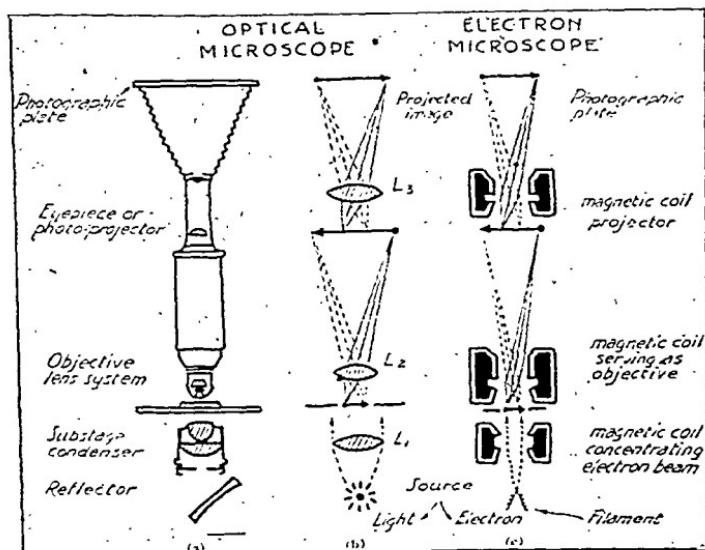
FIG. 1.—Comparison of light microscope and magnetic electron microscope. (Drawings supplied by the Radio Corporation of America.)

H. Busch showed in 1926 that the action of short, axially symmetrical, magnetic fields on electron rays was similar to the action of a glass lens on light rays. It was to be expected that electron optics soon would be used to overcome the limits to microscopy. M. Knoll and E. Ruska in 1932 published their first experimental results on the electron

movements to prevent stiffness of joints are necessary for the fingers when pedicle grafts are transferred from the abdomen or elsewhere by means of the arm; and for the toes when the legs are immobilized for cross leg grafts. Such movements must be commenced immediately after operation and be sufficiently frequent to prevent stiffness. The test of efficiency of the Physical Medicine Department is that stiffness is prevented rather than function restored.

Œdema of a limb due to trauma or hypostasis is troublesome to the plastic surgeon and leads to stiffness of joints. It should be controlled as soon as possible by elevation, frequent massage, static contractions of the large muscle groups of the limb and occupational therapy performed with the limb in the elevated position. As soon as the œdema is under control the dependent position is resumed by graduated stages.

The President expressed surprise at the scant use which was apparently made of physical methods in the preparation of the receptor areas in grafting. Much excellent work done by Nutini and his co-workers had proved beyond dispute that raw areas treated by ultraviolet light were not only sterilized superficially but that the cells damaged by this agent produced substances which provoked proliferation in other cells. It would seem that irradiation with ultraviolet light might be indicated before grafting to ensure taking.

[*June 21, 1944*]

The Electron Microscope: Its Application to Medicine

By G. E. Donovan, M.Sc., M.B., D.P.H.

Function depends on structure. It is also true that structure is altered or moulded by function. Any advance which makes the perception of the finer details of structure possible is of interest to the doctor.

Resolution and Visibility

The resolving power (as apart from magnifying power) of a microscope is its capacity to separate two adjacent points, and this property determines the amount of structural detail that can be observed. The maximum resolving power of the "naked" eye is 0·1 mm. (100 microns). The limit of resolution of the light microscope is attained, using visible light of the shortest wavelength, when the magnification reaches approximately 2,000 diameters. Theoretically, with axial illumination, two points closer together than half the wavelength of the light used cannot be resolved. It is not possible to attain this theoretical limit under normal visual working conditions and, in practice, the limit is reached at about 0·25μ (0·00025 mm.). It is to be remembered that an average human red blood corpuscle is about 7·5μ.

According to Abbe, the smallest distance d of two parts of an object which can be resolved with light of wavelength λ is given by

$$d = \lambda / (n \sin \alpha),$$

where (N sin α) is the numerical aperture of the objective, N being the refractive index of the object space and α the semi-vertical angle of the cone rays entering the objective. If the wavelength λ is decreased, this resolving distance d can be reduced.

Resolution, however, must not be confused with visibility, because it is possible to see "elementary bodies" (of virus diseases) as small as 0·074μ with ordinary white light, and even smaller, 0·0673μ with green light. The difference between visibility and resolution can be illustrated if a printed page be placed about a distance of 10 feet away. It is possible to see that the print consists of a number of letters, but it is not possible to distinguish the form and shape of the actual letters as such at this distance. The letters are visible but their details cannot be resolved.

The ultraviolet microscope.—If ultraviolet light is used instead of visible light, a 50% improvement in resolving power can be obtained, but special quartz lenses and photographic registration must be employed. By this means, J. E. Barnard has succeeded in photographing several of the filterable viruses.

Electron Rays

The limitations imposed when using light radiations have largely been removed as the result of recent progress in electron physics. It has been found that moving electrons behave as if they were associated with a wavelength; this wavelength being an inverse function of their velocity. Some photographs have been published which show diffraction rings produced by light passing through a minute hole in an opaque screen. These rings are due to the fact that light is propagated by wave motion. Other photographs show similar diffraction rings and patterns produced by electrons passing through a thin gold film, and by electrons reflected off a small face of gold. That this does not result from X-rays produced by the electrons striking the gold leaf is proved by the fact

can be replaced by a photographic plate when a permanent record is wanted. The magnification can be varied by manipulation of the electrical controls, and a further enlargement of up to six or seven times these values is obtained by photographic means. Zworykin (1941) and his associates of the R.C.A. have further developed a high voltage electron microscope which uses 300 kv.

THE ELECTROSTATIC ELECTRON MICROSCOPE

Since the beam of cathode-rays can be focused by electrostatic lenses, it is not surprising that models of electron microscopes have been introduced which incorporate this principle. Instead of the magnetic fields produced by coils, electrostatic fields produced by electrically charged diaphragms are employed as electron lenses. As focusing in the General Electric Company instrument is achieved by means of electrostatic instead of electromagnetic fields, the apparatus is smaller and simpler than the electromagnetic model—only a single unregulated voltage to earth is needed. The length of the main tube which is mounted horizontally is only 11 in. from the hairpin-shaped hot cathode to the fluorescent screen, which is viewed and photographed through a glass lens. External photography removes the need of the insertion chamber for the photographic plate. The whole of the energy contained in the electron image is concentrated into a smaller area on the screen, with corresponding greater brightness, while the amount of light gathered by the optical lens from the image on the screen increases with the magnification. A magnification of only × 500 is required from the electron lenses, which, however, can be increased to 7,000 or 8,000 by optical or photographic enlargement before blurring occurs. The instrument requires 35 kv.

ELECTROSTATIC AND ELECTROMAGNETIC MICROSCOPES

The electrostatic lens used in electron microscopy to-day is of the unipotential type, the so-called *einzel-lens*. The focal length of such a lens is fixed. In order to bring the image into focus, the object distance is varied mechanically.

ELECTRONIC ABERRATIONS

Chromatic aberration.—All lens systems, whether they be optical, electromagnetic or electrostatic, are liable to chromatic aberration, and this is due to the radiation, whether visible or not, consisting of mixed wavelengths, which normally come to a focus at different points. Visible light is a mixture of different colours, but the difficulty is compensated to a sufficient extent by employing two different kinds of glass, each having complementary effects on the most important wavelengths. For electron beams, the wave-length is a function of the anode voltage, and can be kept constant by generating the electron rays at exactly the predetermined voltage, and maintaining a high degree vacuum in the tube, to minimize collisions with molecules of residual air. Means are employed in practice for limiting fluctuations to within about $\pm 0.002\%$ of the correct value for the electromagnetic instrument. Chromatic aberration is also due to dissipation of the electron energies in the specimen under examination. As the mass thickness of the usual electron microscope preparation is generally very small, the mean loss of electron energy is also very small.

Spherical aberration.—Spherical aberration sets an all-important limitation for existing electron microscopes. With optical lenses it is minimized, either by the use of a small stop (or aperture), or by an elaborate arrangement of elements in each lens, the former necessitating an exposure varying inversely with the square of the aperture. With electron lenses, there is also a choice between a small stop and a special design of the pole-pieces, or electrodes. The resolving power of an optical microscope depends on having a lens of large numerical aperture. In the electron microscope, however, physical factors compel the opposite course to be followed, or the definition suffers. A very fine cone of rays is all that can be tolerated. A stop, which can transmit less than 1% of the radiation falling on it, and 1/1,000 of an inch in diameter, is employed. This explains why the resolving power of the electron microscope, which, theoretically, should be 100,000 times, is restricted to 50 to 100 times, that of the ordinary microscope.

UNUSUAL ELECTRON MICROSCOPES

Two interesting attempts have been made to obtain electron microscopes of high magnification on rather different and novel lines.

Scanning microscope.—M. v. Ardenne (1938a and 1938b), and Zworykin, Hillier and Snyder (1942) have developed scanning microscopes by applying methods used in television. A magnetic scanning field such as is generally used in television tubes is employed to move an exceedingly fine electron beam "probe" line after line over the surface of the object to be examined. The electrons transmitted through the object (or in other

microscope. They obtained poor pictures and relatively small magnification, but the development of the new technique by E. Ruska, H. O. Muller, H. Krause and others produced gradual improvement. By 1935, the resolving power of the best optical microscope was reached, and in 1937 this was surpassed. B. V. Borries and E. Ruska in 1938 described a technical electron microscope which they designed for the Siemens Company in Berlin. Meanwhile, successful models were developed by L. Marton in Brussels in 1934, L. C. Martin and his associates at the Metropolitan Vickers Company in 1936, and by Prebus and Hillier at Toronto University in 1938. Hillier in 1941 co-operated with Zworykin and Vance of the Radio Corporation of America to produce a commercial and mass-produced electron microscope capable of magnification up to × 150,000. Work on the electron microscope of high magnification was begun in many other laboratories, and only some of the more outstanding contributions are mentioned here.

The Magnetic Electron Microscope

The electron microscope has individual parts serving the purpose of lenses, but these lenses have no material existence, as they are magnetic or electric fields (*see* fig. 2). A
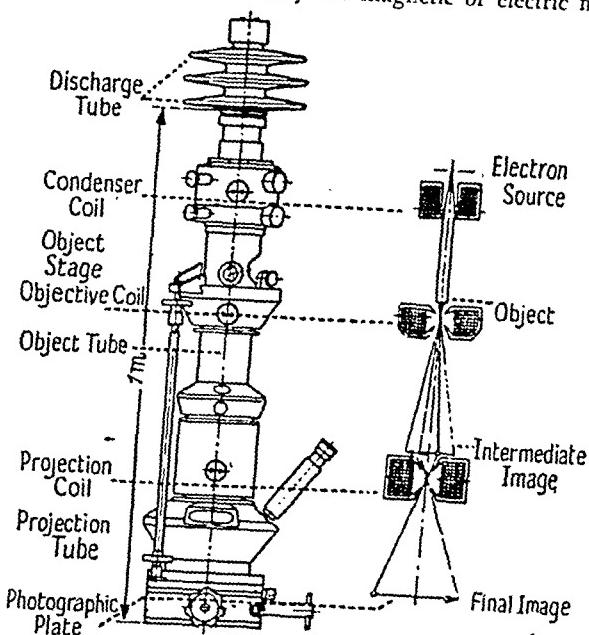
FIG. 2.—Scheme of Siemen's magnetic microscope.

heated filament emits electrons which are accelerated to about 60 kv. *in vacuo*. The actual voltage used depends on the electron wavelength required. The electron rays are concentrated on to the object by means of a focusing magnetic coil. The specimen to be examined is brought into proper position by means of a micrometer adjustment. The electron beam modified by its passage through the specimen is focused by the objective coil and forms an intermediate electron optical image, which is projected on to a fluorescent screen or to a photographic plate by means of a magnetic projection coil. A high speed diffusion pump which maintains high vacuum inside the microscope is incorporated in its stand. The specimen and photographic plates are introduced from outside by means of air-locks, without breaking the main vacuum, so that only a few minutes after their introduction the vacuum is complete enough to use the instrument again. The cathode-rays strike the relatively delicate specimen for the short time of exposure only. For the rest of the time, the beam is deflected by means of a magnetic field set up in the deflection chamber. The magnetic lenses used in the electron microscope have focal lengths of a few millimetres.

The R.C.A. high voltage electron microscope has an upper fluorescent screen upon which the first image is focused, and which can be viewed through one of the upper peep-holes. This enables the required part of the specimen to be located. The main screen can be examined with both eyes through the six ports at the base. This screen

PRACTICAL APPLICATIONS

Until very recently, the electron microscope remained an experimental instrument in the hands of the physicists, and it is only in the last few years that any serious attempt has been made to exploit its possibilities for research. Most of the examinations so far reported have been directed towards the discovery of possible fields of research, rather than towards the solution of particular problems. It holds great promise in almost every field of science, especially in chemistry, metallurgy, medicine and biology, as it reveals many important structural details and reactions, which have hitherto been inaccessible to direct observation and measurements.

Dusts and smokes are among the simplest kind of materials to view in the electron microscope, revealing groups of ultramicroscopic particles that float in the air. This type of research is of interest to the public health worker, and those interested in environmental diseases such as the industrial doctor, &c. A great number of the particles found in human lungs are smaller than 5μ in diameter, and an appreciable number less than 0.2μ. Electron micrographs have been published of smoke particles resulting from the combustion of zinc, magnesium ribbon, aluminium, &c. The physical structure of these differs, and the electron micrograph reveals how magnesium oxide consists of small cubic crystals, aluminium oxide smoke is made up of strings of spherical globules, &c.

Powders are required for many purposes, and a knowledge of their physical structure is of importance. A sample of lead arsenate insecticide which possessed unusual covering power and toxicity showed under the electron microscope—magnification × 56,500—that the particles consisted of extremely thin flakes, which naturally possess a large surface and clinging power. A popular face powder owed much of its popularity to the fact that it did not easily come off. The electron microscope showed that its particles were of a highly angular shape, capable of hooking themselves into the epidermis.

It has many uses in organic chemistry, for instance, an electron micrograph has been published (*Trans. A.I.E.E.*, April 1940), showing a specimen of polyvinylchloride. The magnification × 100,000 shows the specimen to be mottled with an evenly spaced succession of spots. The spots are considered small enough to be of molecular dimensions, and there is little doubt that visual confirmation is here obtained of the truth of the molecular theory. It has been used in the study of protein molecules (Stanley and Anderson, 1942).

It is now possible to obtain electron micrographs of the location of certain chemical reactions incident to the metabolism of the bacterial cell. The reduction of potassium tellurite by *C. diphtheriæ* has been studied (Morton and Anderson, 1941). It has been demonstrated that tellurium crystals form in all parts of the micro-organism, in some cases puncturing its walls. A method of selective microchemical analysis has been developed (Mudd and Anderson, 1942) by taking electron pictures of bacteria after exposure to salts of heavy metals. The electron microscope has demonstrated changes in the bacterial cell brought about by the action of germicides and antibacterial substances (Mudd, 1943). The recording of the action of germicide agents on individual bacterial cells is a promising field of application of microchemical analysis.

Electron micrographs of bacteria have been published (Mudd, Polevitzky and Anderson, 1942). The *Myobacterium tuberculosis hominis* shows that its cell wall appears to be very delicate. Many small dark granules appear throughout the field and, in particular, adhering to the cell wall. Large black granules are shown within the protoplasm. A strain of Fusobacterium shows dense areas, but in contrast to that of the tubercular bacilli the dense areas are not localized in definite circumscribed granules. Monotrichates, for instance, *Vibrio schuylkilliensis*, show a cell wall Definite circumscribed granules are again seen within the protoplasm. The flagella of monotrichates—for example, vibrios—are on the whole wider in diameter than those of peritrichate and lophotrichate species. Unstained diphtheria bacilli show definite polar bodies. *Treponema pallidum* appears to have flagellate processes at various points along its course. The morphology of *Leptospira ictero-hæmorrhagiæ* and *L. canicola* has been investigated (Morton and Anderson, 1943).

If suspensions of streptococci are subjected for a short period to sonic vibrations some of the cells are cytolysed (Sheffield, 1944). These bacteria retain their original outline, but become transparent to the electron beam, appearing as pale grey bodies and contrasting strongly with the opaque normal cell. *B. subtilis*, after subjection to sonic vibrations, shows the flagella to be continuous with the cell wall.

The combination of antibodies with flagellar and somatic antigens has been demonstrated by the electron microscope (Mudd and Anderson, 1941). It has long been known that the bacterial cell wall and flagella of organisms such as the bacilli of typhoid and paratyphoid are altered by the deposition of antibodies, and the combination of

constructions, those reflected from the object) are collected by the plate which is connected with the grid of the input valve of an amplifier. The amplified currents are then applied to the modulator grid of a television tube, which is scanned in synchronism with the electron probe so that the magnified picture of the microscopical specimen can be viewed on the large fluorescent screen of this cathode-ray tube. From pictures obtained in this way it seems that the resolving power of the scanning electron microscope surpasses that of the optical instrument, but the scanning microscopes are still inferior to the highly developed projection electron instruments.

Shadow electron microscope.—Another type of electron microscope with high magnification is realized in the point-projector or shadow microscope. There the specimen to be examined is brought very close to a minute electron source, casting an electron shadow on to a relatively distant fluorescent screen. The main problem in the method is the production of the point electron source. G. A. Morton and E. C. Romberg (1939) used etched tungsten points of less than 5×10^{-5} cm. as cathodes in their point-projector microscope. H. Boersch (1939a and 1939b), in his shadow microscope, uses two stages of electrostatic lenses in order to reduce the electron optical image of a hairpin cathode. He thus obtained an electron source of minute dimensions. This type of shadow microscope is better than the scanning microscope of v. Ardenne, but still is inferior to the projection electron microscopes.

Characteristics of Electron Micrographs

The chief advantage of the electron microscope is its great resolving power, but sufficient has been said about this property.

Electron micrographs may be considered analogous to X-ray pictures, inasmuch as the darkness and brightness depend on the thickness and density of the specimen as distinct from micrographs obtained with the light microscope where an image is formed due to differences in the amount of absorption or refraction within the object. The presence of very small particles in specimens for examination under the electron microscope will cause perceptible scattering, and the image formed of an object thicker than about 0.5μ is merely an enlarged silhouette.

Another characteristic, which is usually an advantage, is the great depth of focus. This is useful for stereoscopic work.

Specimen Mounting

The vast majority of microscope specimens must be mounted upon a transparent support. Glass of a convenient thickness is the most suitable material when the illuminant is visible light, but it is opaque to an electron stream, and a new technique has therefore been elaborated whereby specimens may be adequately prepared for examination. A very thin, uniform film of collodion or nitrocellulose is used. It produces a uniform diminution of intensity, and if the film is thin enough, the amount of scattering and spread of velocity caused by it does not cause much interference with the picture. A very thin film is obtained by dropping a small quantity of a 1·5% solution of collodion in amyl acetate on amyl-acetate-saturated water. The film spreading over the surface is taken up and dried on a small circular disc of 200-mesh wire gauze, less than ⅛ in. in diameter. Gentle pressure on the diaphragm causes it to adhere to the film. Films of this kind are thinner than the length of a collodion molecule. The coated discs are separated from the rest of the membrane by means of delicate handling tools, lifted from the water, inverted so as to bring the film side uppermost, and placed upon a miniature pedestal. There the water clinging to the surface is removed, and a drop of a fluid containing the specimen in suspension or solution is placed upon it, and the fluid allowed to evaporate. The whole is then placed in position on the cartridge, which in its turn is inserted through the air-lock into the microscope tube's interior, i.e. into the space about to be evacuated.

Casts of specimens.—The surfaces of certain materials, for instance, metals and alloys, can be studied by light reflected from them in the optical microscope, but this is generally impracticable with electron rays. A cast of the surface can be made by using some sort of plastic in solution and allowing the solvent to evaporate: a negative solid replica of the surface structure can be produced by peeling off the film from the original, and can be examined like an ordinary specimen in the electron microscope. An electron image of such a film will develop more strongly where the plastic material is thinnest. In some cases, where a replica cannot be stripped off, satisfactory results can be got by dissolving the original in some acid or other solution which the plastic film can withstand. The cast technique may be useful for examining the surface of such structures as metals, teeth, &c.

enced in viewing anything but "dead" specimens, and in consequence, movement must inevitably be "frozen", and require a number of successive and similar operations to show progressive action. The objects to be examined must be extremely thin.
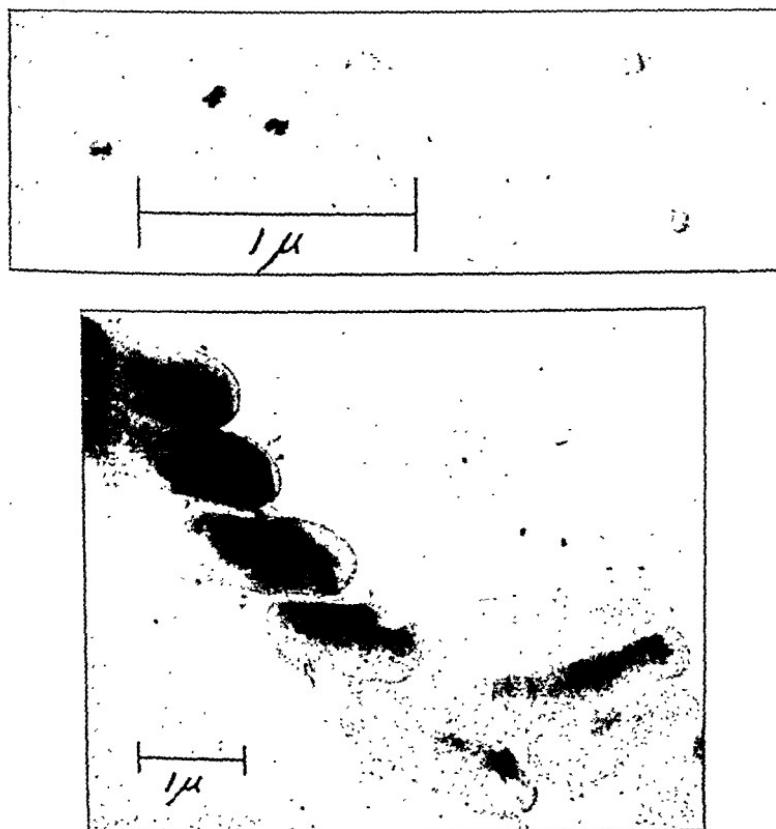
FIG. 3.—Bacteriophage. The lower picture shows bacteriophage attacking *B. coli.* (*From* " The Identification and Characterization of Bacteriophages with the Electron Microscope," by S. E. Luria and T. F. Anderson, *Proceedings of the National Academy of Sciences of the United States of America,* 1942, 28, 127.)

SOME FURTHER DEVELOPMENTS

Owing to the very small aperture of the electron rays, the electron microscope shows a surprisingly large depth of focus. Electron stereomicroscopy has been suggested by E. Ruska. M. v. Ardenne (1940) has further developed this idea. and introduces in his electron microscope a particular object carrier which can be tilted by a few degrees between two successive exposures. A vivid impression of solidity is produced if the two corresponding photographs are examined under a stereoscope.

M. v. Ardenne (1940) has successfully applied dark-ground illumination and obtained resolving powers down to 5×10^{-7} cm. M. v. Ardenne (1939) discusses in this connexion the possibility of viewing single atoms, and studying their distribution in the object plane. There are, however, great practical difficulties, for instance, the exposure time would have to be increased more than 1,000 times if ultramicroscopical methods were to be introduced.

O. Scherzer (1939) discusses the possibility of improving the resolving power of the ordinary electron microscope with direct illumination by an improvement of the electron lenses leading to larger numerical apertures. He mentions in this connexion the practicability of correcting spherical abberation by introducing space charges into the lens. F. H. Nicoll in his patent proposal of 1936 discusses the introduction of an electron mirror into the instrument. As it is feasible to construct mirrors with negative aberration, a useful opportunity of correcting the mirror-microscope is given.

antibodies and antigens at bacterial surfaces has also been shown by quantitative analytical methods. These sensitized surfaces have now been examined under the electron microscope, and, as a result of the deposition of homologous antibodies upon them, the walls are found to become opaque, and less clear-cut in outline. The flagella become thicker, but less sharp and less uniform in outline, and they tend to coalesce.

The various viruses differ greatly in size, although each kind of virus is itself very uniform in size. During the last decade, a few of the viruses which attack plants have been isolated. Although they differ from each other in stability and analytical composition, all those purified have been shown to consist solely of nucleoproteins of high molecular weight. These viruses seem to be a connecting link between living and non-living matter. They are actually protein molecules possessed of certain definite biological acitivity. On the other hand, there are viruses, that of vaccinia, for example, and all the Rickettsia disease agents, which are very much larger, and cannot be regarded as single molecules. The larger viruses appear to be true micro-organisms which can only live a parasitic existence. One of the first viruses to be photographed under the electron microscope was that of tobacco mosaic, and it at once confirmed the suggestions, based on other methods, about the size and shape of this virus. It was a long rod about 300 mµ. Particles of tobacco mosaic virus appear in purified form as discrete rod-like units with a tendency to side-to-side and end-to-end aggregation. The electron microscope has also been used in the study of the virus of tomato bushy stunt. The reaction between tobacco mosaic virus and its antiserum has been studied by means of the electron microscope (Anderson and Stanley, 1941). This instrument has been used in the investigation of the morphological structure of the virus of vaccinia (Green, Anderson and Smadel, 1942). The elementary bodies of vaccinia are rectangular shaped, resembling a brick, and contain five areas of condensation, and are somewhat like the five spots of a dice. Sharp (1942b) and his colleagues have employed the electron microscope in their investigations of western strain equine encephalomyelitis virus. Taylor (*see* Sharp *et al.*, 1942c) and his associates have used this instrument on the eastern strain equine encephalomyelitis virus. Studies have been published (Chambers and Henle, 1943) on the nature of the virus of influenza with particular reference to the dispersion of the virus of influenza A in tissue emulsions, and in extra-embryonic fluids of the chick. The size of the infectious unit in influenza A has been investigated (Chambers, Henle and their associates, 1943). This instrument has been employed on the morphological structure of Rickettsiæ (Plotz, Smadel and Anderson, 1943). It has also been used in studies on the papilloma virus protein (Sharp, Taylor *et al.*, 1942a).

Studies of bacteriophages (Luria and Anderson, 1942) disclose an extremely constant and characteristic sperm-like appearance with a round head, and a much thinner tail: in many micrographs the head is filled with a dense internal structure (fig. 3). These are adsorbed to their specific micro-organisms by head or tail, and after contact it is possible to observe extensive damage of the bacterial cell. These results are interesting, as some years ago the bacteriophage was looked upon by some workers as of macromolecular nature. The discovery of such constant and detailed information is of interest also to geneticists, for genes are thought to be macromolecular entities. The sperms of the ram and bull, being extremely flat, lend themselves to examination and have already come under observation.

The electron microscope is of value in histological research. It has revealed characteristic cross-striations in collagen fibres, and the effects of various physical and chemical conditions on the fibres have been investigated (Hall, Jakus, and Schmitt, 1942) in a search for further knowledge of the molecular structure of collagen. To entomologists, this instrument shows hitherto unseen structures, and it allows the accurate measurement of those already recognized. The tracheæ, trachioles, air sacs, wing scales, and cuticle have been examined, and experiments (Richards and Anderson, 1942) on the mode of penetration of the cuticle by non-volatile oils serve as an example of future useful applications.

The foregoing are only some of the many fields in which an electron microscope is useful.

SOME DISADVANTAGES

The electron microscope is not yet an instrument for every pathologist's bench, due to its cost, size and complexity. Its immediate future lies rather in the research laboratory. The bombardment of specimens with high speed electrons produces changes in protoplasm, and in molecules. Entomologists have remarked on shrinkage, evolution of gas, discoloration, and increased friability of their specimens. As the specimen for study must be placed in a high vacuum, it must, therefore, be dry. Great difficulty is experi-

Section of Radiology

President—N. S. FINZI, M.B.

[January 21, 1944]

DISCUSSION ON RADIOTHERAPY IN CHRONIC INFLAMMATORY CONDITIONS WITH SPECIAL REFERENCE TO MYCOTIC INFECTIONS

Squadron Leader Alexander B. MacGregor *[Abridged]*: The ætiology of actinomycosis was discussed and it was pointed out that the work of Erikson, 1940, had shown that the organism causing lesions in the human was distinct from the bovine type. The work of Naeslund, 1925, Lord, 1933, Emmons, 1935, and others, had also shown the presence of anaerobic strains corresponding in morphological and cultural characteristics to the organism causing human lesions in normal mouths. There were therefore no grounds for the continuation of the supposition that human actinomycosis had any association with cattle or agriculture. It appeared more probable that the normal saprophytic organism could become parasitic under certain circumstances. e.g. local trauma. The association of actinomycosis of the cervico-facial region with dental extractions, particularly in the lower molar region, was noted. The mode of spread of the organisms was discussed and the theory of a lymphatic block followed by thrombo-phlebitis was advanced to account for the curious fact that an organism apparently gaining entry via a tooth socket did not primarily involve the bone or the lymph nodes, but the soft tissues of the cervico-facial region.

The various methods of treatment were outlined and the necessity for surgical principles of drainage, &c., was stressed, as were the dangers and difficulties of radical surgery in the cervico-facial region. Particular attention was given to the use of sulphonamides and also to the use of penicillin during treatment of the disease. Suspensions of sulphonamides, particularly those with slower absorption, such as sulphapyridine and sulphathiazole, had been used locally on packs and by injection with some measure of success. The majority of organisms from human cases of actinomycosis had proved very insensitive to penicillin. One case however was described in which the organism was considerably more sensitive than the control staphylococcus. This case had been treated by local penicillin with apparently very successful results. Fallacies in checking the results owing to difficulty in culture of the organism, and the length of time that must be allowed to elapse before a cure is claimed, were stressed. The fact that most strains so far encountered were insensitive to penicillin, while one was very sensitive, coupled with much other evidence, strongly suggested that many strains of the human *A. israeli* type were probably erroneously regarded as being one, and further work was required for their separation. Radiotherapy appeared to offer good possibilities in many cases and the speaker advocated a combination of radiotherapy, surgery and chemotherapy to obtain the optimum result.

Dr. John Blewett: The following conditions are among those in which radiotherapy has been found of value.

Chronic pyogenic infections: Superficial inflammatory diseases of the skin and sub-cutaneous tissues, for example, chronic furunculosis respond to a single dose of from 200 to 300 r, or to repeated doses of the same size given at intervals of two to three weeks.

The most direct method of improving the resolving power is to use appreciably greater electron energies, and thus shorter wavelengths. There is an upper limit to what we can hope for in this direction.

After this war is over, there should be great development in television, and some of this research work will be employed in improving the electron microscope.

My thanks are due to the Research Departments of the Radio Corporation of America; the General Electric Company of America; Metropolitan Vickers of England; Mr. G. Parr, Editor of *Electronic Engineering;* Dr. P. Bauwens, President of the Physical Medicine Section of the Royal Society of Medicine; Mr. T. J. Shields, Librarian of the British Medical Association; and Mr. C. F. Home, Librarian of the Royal Society of Medicine.

REFERENCES

ANDERSON, T. F., and STANLEY, W. M. (1941) " A Study by Means of the Electron Microscope of the Reaction between Tobacco Mosaic Virus and its Antiserum," *J. Biol. Chem.,* **139,** 339.
v. ARDENNE, M. (1938a) *Z. tech. Phys.,* **19,** 407.
—— (1938b) *Z. Phys.,* **108,** 338.
—— (1939) *Z. Phys.,* **112,** 744.
—— (1940) *Z. Phys.,* **115,** 339.
BOERSCH, H. (1939a) *Naturwissenschaften,* **27,** 418.
—— (1939b) *Z. tech. Phys.,* **20,** 346.
CHAMBERS, L. A., and HENLE, W. (1943) " Studies on the Nature of the Virus of Influenza I. The Dispersion of the Virus of Influenza A in Tissue Emulsions and in Extra-Embryonic Fluids of the Chick," *J. exp. Med.,* **77,** 251.
——, ——, LAUFFER, M. A., and ANDERSON, T. F. (1943) " Studies on the Nature of the Virus of Influenza II. The Size of the Infectious Unit in Influenza A," *J. exp. Med.,* **77,** 265.
GREEN, R. H., ANDERSON, T. F., and SMADEL, J. E. (1942) " Morphological Structure of the Virus of Vaccinia," *J. exp. Med.,* **75,** 651.
HALL, C. E., JAKUS, M. A., and SCHMITT, F. O. (1942) " Electron Microscope Observations of Collagen," *J. Amer. chem. Soc.,* **64,** 1234.
LURIA, S. E., and ANDERSON, T. F. (1942) " Identification and Characterization of Bacteriophages with the Electron Microscope," *Proc. nat. Acad. Sci. Wash.,* **28,** 127.
MORTON, G. A., and ROMBERG, E. F. (1939) *Phys. Rev.,* **56,** 705.
MORTON, H. E., and ANDERSON, T. F. (1941) " Electron Microscope Studies of Biological Reactions; Reduction of Potassium Tellurite by *Corynebacterium Diphtheriæ,*" *Proc. Soc. exp. Biol., N.Y.,* **46,** 272.
——, —— (1943) " Morphology of *Leptospira ictero-hæmorrhagiæ* and *L. canicola* as revealed by the Electron Microscope," *J. Bact.,* **45,** 143.
MUDD, S. (1943) " Changes in the Bacterial Cell Brought about by the Action of Germicides and Antibacterial Substances as demonstrated by the Electron Microscope," *Amer. J. publ. Hlth.,* **33,** 107.
——, and ANDERSON, T. F. (1941) " Demonstration by Electron Microscope of Combination of Antibodies with Flagellar and Somatic Antigens," *J. Immunol.,* **42,** 251.
——, —— (1942) " Staining for Electron Micrography ; Effects of Heavy Metal Salts in Individual Bacterial Cells," *J. exp. Med.,* **76,** 103.
——, POLEVITZKY, K., and ANDERSON, T. F. (1942) " Bacterial Morphology as shown by Electron Microscope ; Structural Differentiation within Bacterial Protoplasm," *Arch. Path. Lab. Med.,* **34,** 199.
PLOTZ, H., SMADEL, J. E., and ANDERSON, T. F. (1943) " Morphological Structure of Rickettsiæ," *J. exp. Med.,* **77,** 355.
RICHARDS, A. GLENN., Jr., and ANDERSON, T. F. (1942) " Electron Microscope Studies of Insect Cuticle with a Discussion of the Application of Electron Optics to this Problem," *J. Morph.,* **71,** 135.
SCHERZER, O. (1939) *Z. Phys.,* **114,** 427.
SHARP, D. G., TAYLOR, A. R., BEARD, DOROTHY, and BEARD, J. W. (1942a) " Study of the Papilloma Virus Protein with the Electron Microscope," *Proc. Soc. exp. Biol., N.Y.,* **50,** 205.
——, ——, ——, —— (1942b) " Electron Micrography of the Western Strain Equine Encephalomyelitis Virus," *Proc. Soc. exp. Biol., N.Y.,* **51,** 205.
——, ——, ——, —— (1942c) " Electron Micrography of the Eastern Strain Equine Encephalomyelitis Virus," *Proc. Soc. exp. Biol., N.Y.,* **51,** 332.
SHEFFIELD, F. M. L. (1944) " The Electron Microscope and its Use in Biological Research," *Sch. Sci. Rev.,* **25,** 201.
STANLEY, W. M., and ANDERSON, T. F. (1942) " Electron Micrographs of Protein Molecules," *J. biol. Chem.,* **146,** 25.
ZWORYKIN, V. K., HILLIER, J., and VANCE, A. W. (1941) " A Preliminary Report on the Development of a 300-kv Magnetic Electron Microscope," *J. appl. Phys.,* **12,** 738.
——, ——, and SNYDER, R. L. (1942), " A Scanning Electron Microscope," *A.S.T.M. Bull.,* August.

Section of Radiology

President—N. S. FINZI, M.B.

[*January* 21, 1944]

DISCUSSION ON RADIOTHERAPY IN CHRONIC INFLAMMATORY CONDITIONS WITH SPECIAL REFERENCE TO MYCOTIC INFECTIONS

Squadron Leader Alexander B. MacGregor [*Abridged*]: The ætiology of actinomycosis was discussed and it was pointed out that the work of Erikson, 1940, had shown that the organism causing lesions in the human was distinct from the bovine type. The work of Naeslund, 1925, Lord, 1933, Emmons, 1935, and others, had also shown the presence of anaerobic strains corresponding in morphological and cultural characteristics to the organism causing human lesions in normal mouths. There were therefore no grounds for the continuation of the supposition that human actinomycosis had any association with cattle or agriculture. It appeared more probable that the normal saprophytic organism could become parasitic under certain circumstances. e.g. local trauma. The association of actinomycosis of the cervico-facial region with dental extractions, particularly in the lower molar region, was noted. The mode of spread of the organisms was discussed and the theory of a lymphatic block followed by thrombo-phlebitis was advanced to account for the curious fact that an organism apparently gaining entry via a tooth socket did not primarily involve the bone or the lymph nodes, but the soft tissues of the cervico-facial region.

The various methods of treatment were outlined and the necessity for surgical principles of drainage, &c., was stressed, as were the dangers and difficulties of radical surgery in the cervico-facial region. Particular attention was given to the use of sulphonamides and also to the use of penicillin during treatment of the disease. Suspensions of sulphonamides, particularly those with slower absorption, such as sulphapyridine and sulphathiazole, had been used locally on packs and by injection with some measure of success. The majority of organisms from human cases of actinomycosis had proved very insensitive to penicillin. One case however was described in which the organism was considerably more sensitive than the control staphylococcus. This case had been treated by local penicillin with apparently very successful results. Fallacies in checking the results owing to difficulty in culture of the organism, and the length of time that must be allowed to elapse before a cure is claimed, were stressed. The fact that most strains so far encountered were insensitive to penicillin, while one was very sensitive, coupled with much other evidence, strongly suggested that many strains of the human *A. israeli* type were probably erroneously regarded as being one, and further work was required for their separation. Radiotherapy appeared to offer good possibilities in many cases and the speaker advocated a combination of radiotherapy, surgery and chemotherapy to obtain the optimum result.

Dr. John Blewett: The following conditions are among those in which radiotherapy has been found of value.

Chronic pyogenic infections: Superficial inflammatory diseases of the skin and subcutaneous tissues, for example, chronic furunculosis respond to a single dose of from 200 to 300 r, or to repeated doses of the same size given at intervals of two to three weeks.

Osteomyelitis: Where the course of the disease is prolonged and reparation is delayed similar doses of X-rays will expedite recalcification. Transient local reactions have been observed, but they have not led to undesirable after-effects.

Chronic mastitis often yields to small repeated doses at bi-weekly intervals but the results are variable, possibly because the total dose has been deliberately kept at the lower levels.

Tuberculous adenitis: A course of 600 to 900 r subdivided over two weeks hastens resolution of the affected glands and lessens the need for surgical interference. This course is repeated two or three times in a year and accompanied by general medical treatment.

Chronic arthritis: The effects of radiation on a group of nearly 300 unselected cases of chronic non-specific arthritis were studied over a period of some years and of them 35% showed considerable and lasting improvement. All forms of the disease responded to a like extent. The X-ray appearance of the joint remained unchanged or showed a slowly progressive deterioration despite a marked absence of pain and, comparatively, of disability.

Ankylosing spondylitis was one type in which treatment in the early stages was followed by consistently good results.

Mycotic infections: These comments are based on a group of 58 cases recorded within ten years, the most recent having a period of at least six months' observation. 36 were treated by X-ray in addition to other methods, the remainder received no radiation.

All but 3 were confirmed infections of actinomycosis, 1 of the others was a blastomycosis, and in the remaining 2 the diagnosis was made on clinical evidence only.

CERVICO-FACIAL INFECTION—39 CASES			ABDOMINAL INFECTION—16 CASES		
Treated with X-ray		29	Treated with X-ray		7
Free of signs of disease ...	25		Free of signs of disease ...	1	
Relapsed and required subsequent surgical treatment	1		Died of the disease ...	4	
			Still under treatment ...	1	
No record available ...	3		No record available ...	1	
Treated without X-ray ...		10	Treated without X-ray ...		9
Free of signs of disease ...	6		Free of signs of the disease	5	
No record available ...	4		Improved but still affected	1	
No deaths were recorded in this group.			Died of the disease ...	2	
			No record available ...	1	

The 3 remaining cases were infections of rare sites, 2 with metastatic abscesses and 1 of the breast successfully treated by mastectomy.

Comments.—Many of the cases recorded as having been treated by radiotherapy had received either surgical or chemotherapeutic treatment previously and were only referred for X-ray when these methods had had no conclusive result. The numbers are necessarily small and in themselves of little value in comparing the efficiency of particular forms of treatment. While the results in the cervico-facial group are very satisfactory, the abdominal infections, in our hands, show a considerable mortality which has not been lessened to any extent by radiation. In the cervico-facial group, where the lesion is open to direct observation, X-ray is followed generally by a rapid and complete resolution and in contrast to those not so treated rarely requires further surgical incision.

The dose used was in the neighbourhood of 300 r as a single exposure which was repeated at intervals of three weeks according to the clinical indications until all induration had disappeared. More intensive treatment was accompanied by a greater tendency to abscess formation and possible damage to the skin. Variations of dose both larger and smaller did not lessen the period of convalescence, the average time taken for a complete cure being about three months.

No entirely satisfactory theory has been advanced to explain the mode of action of X-ray in these infections. All experimental work indicates a destructive action on organic life, a selective destruction which gives a rational basis for treatment Results may be achieved by such an action on either the infecting organism or on inflammatory cells of the host. The former is generally not entertained as the order of dosage necessary to affect bacteria *in vitro* experiment is so far in excess of that used in therapy. Some evidence is available to indicate in the fungi a wider variation of sensitivity. The more widely held theories attribute the action of radiation to the sensitivity of some cellular element of the inflammatory aggregate In the chronic conditions under review immature fibroblastic tissue is suggested as a likely recipient as it is so constantly

present and its development is suppressed by tissue doses of the order of those found to be most efficient in the treatment of these diseases.

Mr. I. G. Williams (Middlesex Hospital): Actinomycosis simulates malignant disease in that early diagnosis and localized extent will lead to cure without deformity whilst wide involvement causes crippling deformity, ankylosis of joints and death. Although the administration of potassium iodide has recently been discredited, we believe that given in large enough doses the duration of the disease is shortened. Starting with mist. pot. iod. (gr. 10) we increase by 5 gr. per dose daily to gr. 90 t.d.s. Pot. citrate gr. 30 given at the same time diminishes the tendency to iodism. Only one of our cases developed iodism. Potassium iodide is prescribed in diminishing doses as the disease becomes less active and continued for one month after healing. Sulphonamides are prescribed according to the clinical condition and the nature of the secondary infection. One case of pelvic abscess responded to M & B 693 given by mouth together with incision and drainage. He remains well after six years.

Radiotherapy.—This forms the most useful single therapeutic measure available to-day, and although radium therapy may be used, X-ray therapy is simpler and more efficacious. In our practice intensive fractionated therapy with a hard ray H.V.L. (1·3 mm. Cu) gave the best results. Small daily doses 100 r to 150 r (w.b.s.) to a total of 2,500 r (w.b.s.) in twenty-four to twenty-eight days were given over fields sufficient to cover the whole of the involved area. Tissue dose is difficult to assess but it appeared from the localized type that 2,000 r delivered to the affected tissue in twenty-eight days was satisfactory. *The mode of action of radiotherapy* is difficult to assess. Three possibilities occur: (1) Desjardins' theory of the liberation of antibodies from disintegration of leucocytes locally under the influence of radiations. (2) Vasodilatation. (3) Direct lethal effect on the organism. One case suggested this. Female, aged 52, with pelvic actinomycosis. There were abundant mycelia in pus from sinuses. She died after 1,500 r had been delivered to the affected tissues in eighteen days. Post mortem: Numerous samples of pus from the same sinuses and pelvis were negative for the organism.

Complications.—The main one was false ankylosis of the jaw. The use of cones, gags and props during therapy may prevent this.

Statistics: 43 cases, 30 M., 13 F., ages average 39 years. Youngest 12 years, oldest 65 years. Localities: All London boroughs and counties of South England represented. 6 or 14% were associated with animals or agriculture. Clerks, housewives, salesmen, school-boys, and soldiers made up the rest. From 1937-42 yearly incidence was 3 to 6 cases. In 1943, 11 patients were seen, 6 of these being serving soldiers.

Location.—Cervico-facial 60·5%; right iliac fossa 27·9%; pleuropulmonary 4·7%; rare sites 7·0%; one ovarian abscess: one perinephric abscess. Mortality 6, untraced 7 (4 followed up over twelve months)

TABLE I.

	No.	Cured	Died of disease	Untraced
Cervico-facial	26	23	—	3
Right iliac fossa	12	5	3	4
Pleuro-pulmonary	2	1	1	—
Other sites	3	1	2	—

Period of observation varies from one to eleven years the majority being over three years. The average length of time from commencement of treatment until clinical cure was ten weeks—the shortest being six weeks and the longest six months.

Dr. Finzi: Both in actinomycosis and in tuberculosis I used to employ much bigger doses of radiation, but there was always a proportion of cases in which I could get no result at all even though they appeared to do well at the beginning of the treatment. In a paper at the Stockholm Congress it was shown that small doses were definitely better in tuberculosis and since then I have reduced the dose still further, aiming at 50 to 60 r at the lesion in an adult and less in proportion in children. The results are much better and there is no danger of skin changes, even if one has to go on for a long time.

In actinomycosis it has been said that it did not matter whether radium or X-rays is used, but I think that probably radium gives rather better results if one can get an adequate dose to the deepest part of the disease without giving the skin a big dose.

Squadron Leader MacGregor has probably given the correct reason why some cases do not respond, in that they may have different varieties of actinomycosis.

DISCUSSION ON THE RADIOTHERAPY OF MALIGNANT DISEASE OF THE OVARY

Mr. Alan Brews (*Summary*): The ovary is the second commonest site of malignant disease in the female genital tract (and the third commonest in the whole female body).

Radiosensitivity is likely to vary widely in the very numerous histological types.

The insidious progress often resulting in widespread dissemination handicaps alike surgical and ray therapy.

Exploratory laparotomy is a necessary adjunct to diagnosis in the vast majority of cases. Pure surgery, combined surgery and radiotherapy and pure radiotherapy all have their province in treatment, but, in general, surgery should be subordinated to radiotherapy rather than vice versa.

Post-mortem material stresses the importance of the naked-eye study of the disease as well as of its cellular structure.

The remote prognosis of surgical treatment alone is very poor.

TABLE I.—INCIDENCE OF MALIGNANT DISEASE OF THE OVARY IN THE LONDON HOSPITAL (1916-1929).

Total neoplasms of ovary, including endometrioma, excluding
retention cyst 1,007
Neoplasms classified as malignant 257
(Based on histological reports) (25·4%)
Neoplasms classified as possibly malignant 24
(2·4%)

Relative incidence of malignant disease in genital tract—
Cervix uteri, 44 a year; Ovary, 18 (plus 2 ?); Corpus uteri, 12.
It would appear that about 1 in 4 of all ovarian neoplasms (not of all ovarian swellings) are malignant (cf. Wilfred Shaw (1932) 300 consecutive ovarian neoplasms—over 27% were malignant; Blair Bell and Datnow (1932) in a series of 2,603 cases, 22·6% were malignant).

TABLE II.—PATHOLOGICAL TYPES.

Primary
Cystadenoma serosum papillare with secondary malignant metaplasia.
Cystadenoma pseudomucinosum with secondary malignant metaplasia.
Dermoid cyst with secondary malignant metaplasia.
Malignant neoplasms de novo, dysgerminoma, arrhenoblastoma, granulosa-celled, malignant teratoma, carcinoma solidum, sarcoma.

Secondary
Transperitoneal implantation.
Retrograde lymphatic permeation.

Indeterminate
20%.

The relative frequency of these types is more difficult to assess as many are mixed or atypical malignant metaplasia of a benign cyst 60%, secondary 20%, indeterminate 20%.

TABLE III.—CLINICAL TYPES.

(1) Generalized carcinomatosis peritonei (±other metastases).
(2) Fixed abdomino-pelvic mass.
(3) Mobile abdomino-pelvic mass : macroscopic signs of malignancy.
(4) Mobile abdomino-pelvic mass : macroscopically benign—microscopically malignant.
(5) Apparently benign neoplasm removed, followed by clinical recurrence.
(6) Recurrence after surgical removal.

SYMPTOMS AND SIGNS OF MALIGNANT DISEASE OF THE OVARY

I have classified the London Hospital cases into 5 groups (Table III). Recurrences form a sixth group which may be secondarily derived from cases originally listed in any of the others.

The only points relevant to this discussion are:

(1) In about one-third of the cases distinction between benign and malignant neoplasm is made pathologically after removal of the tumour or malignancy is only suspected after the abdomen has been opened.

(2) In a further third fixity of the abdomino-pelvic mass makes complete operable removable very problematic before surgery is undertaken.

(3) In the remaining third the disease is so widespread when first seen that surgeon and radiotherapist are uncertain as to the line of treatment.

The Factors Influencing Treatment for Malignant Disease of the Ovary

(1) Anatomically the ovary has a pedicle so that removal for disease confined to the substance of the ovary is one of the simplest in surgery.

(2) Anatomically its lymph drainage is mainly to the juxta-aortic lymphatic nodes in front of the upper three lumbar vertebræ. They are relatively inaccessible to surgical removal and this is rarely attempted. Lesser drainage across the fundus of the uterus to the ovary of the opposite side probably increases when the primary drainage route is permeated with growth. Hysterectomy and bilateral salpingo-oöphorectomy will eradicate this subsidiary lymphatic field.

(3) Physiologically, with the surgical removal of only one ovary, normal sex hormone balance and the reproductive function are retained.

(4) Diagnostically I would make a very strong plea for the necessity of exploratory laparotomy in the majority of cases: (a) It sometimes corrects gross errors in diagnosis, (b) allows of much fuller orientation of characters and extent of the disease, (c) allows of a biopsy for histological examination and as permanent proof of the disease, (d) frequently distinguishes between primary and secondary disease thereby modifying the policy to be adopted, (e) allows of complete paracentesis to the temporary relief of the patient. If the radiotherapist cannot be present at laparotomy, he should be provided with a complete verbal and diagrammatic picture of the character and extent of the disease.

TABLE IV.—POST-MORTEM FINDINGS IN MALIGNANT DISEASE OF THE OVARY.
Gordon Ley, The London Hospital (1909-1919).

Port-mortems on women with carcinoma	...	...	...	...	324
Ovary affected by carcinoma	...	...	...	...	60 (18·5%)
Of these primary ovarian carcinoma	...	...	...	...	25
16 Wolffian					
9 Pseudomucinous					
Of these secondary ovarian carcinoma	...	...	...	...	35
25—no clinical enlargement of ovary					
10—clinical enlargement					

TABLE V.—CONTRAST OF POST-MORTEM FINDINGS IN WOLFFIAN AND PSEUDOMUCINOUS PRIMARY CARCINOMA OF OVARY.
Gordon Ley, The London Hospital (1909-1919).

					Wolffian (16)	Pseudomucinous (9)
Average age	...	...	...	...	54	44
Bilateral	...	...	...	...	8 16	1 9
Peritoneal metastasis	...	...	...	15 16	5, 9
Lymphatic node metastasis	...	...	...	12 16	nil
Lumbar 11 ; cœliac 9 ; iliac 8 ; inguinal 4 ; thoracic 5 ; axillary 3 ; cervical 1.						

In order to compare the results of different forms of treatment Montgomery and Farrell group their cases as follows:

Stage I.—Tumour confined to ovary, no adhesions, no enlarged lymph nodes or other metastases.

Stage II.—Tumour involving other surrounding structures surgically removable *en bloc*, e.g. adhesions, omentum, uterus, other ovary, sometimes part of bowel.

Stage III.—Tumour involving other surrounding structures, growth not completely removable surgically. Involvement of lymph nodes, large vessels, bone, bowel.

Stage IV.—Tumour irremovable: (a) Gross cachexia precluding surgical procedures, (b) extensive local spread and distant metastases.

The Prognosis of Malignant Disease of the Ovaries

Owing to present conditions I cannot supply complete and accurate figures from the London Hospital material. Instead I will quote Schleyer's figures for surgical treatment from the first Frauenklinik, Vienna.[1]

[1] SCHLEYER from v. PEHAN, H., and AMERICH, J. (1930) Gynäkologische Operationslehre, Berlin.

Table VI—Refers to sixteen years (1910—1925) average of 7·2 per year. 15% total malignancy low because retention plus inflammatory cysts included in census.

Table VII—Two-thirds pseudomucinous plus one-third papillary in this group. Wilfred Shaw: "If a tumour is bilateral, 5 to 1 chance it is malignant."

Table VIII—12 deaths in 115 cases = 14% mortality. It is pertinent to ask in this connexion whether a primary mortality and morbidity exists in the case of radiotherapy?

Table IX—The carcinomatous pseudomucinous cyst is the most benign, with the least tendency to metastasis, and implantation, whereas the metastatic is the most malignant in this respect.

The absolute cure figure is very poor, 9·52%.

TABLE VI.
SURGICAL TREATMENT OF MALIGNANT DISEASE OF THE OVARY.
Schleyer's Statistics : 1. Frauenklinik, Vienna.

Total ovarian tumours about 750
Malignant ovarian tumours 115 (15·3%)
Classification :

Malignant pseudomucinous cystomata	23
Malignant papillary cystomata	49
Genuine solid carcinomata...	30
Metastatic enterogenous carcinomata	13
	115

TABLE VII.
Schleyer's Statistics : 1. Frauenklinik, Vienna.

Of the carcinomatous pseudomucinous cystomata :
  15 (65%) were simple*   14 (60·8%) were unilateral
  8 (35%) were extensive   9 (39·2%) were bilateral
Of the malignant papillary cystomata :
  18 (36·7%) were simple*   20 (40·8%) were unilateral
  31 (63·3%) were widespread   29 (59·2%) were bilateral
Of the genuine solid carcinomata :
  8 (26·7%) were simple   14 (46·6%) were unilateral
  22 (73·3%) were extensive   16 (53·4%) were bilateral
Of the metastatic ovarian carcinomata :
  1 (7·6%) was simple   1 (7·6%) was unilateral
  12 (92·4%) were widespread   12 (92·4%) were bilateral

  *Simple = confined to the ovary alone.

TABLE VIII.
Schleyer's Statistics : 1. Frauenklinik, Vienna.

Immediate prognosis :
  18—exploratory laparotomy : immediate mortality nil.
  39—removal : disease clinically limited to ovary : immediate mortality 1 (2·56%).
  58—incomplete removal : metastases or implantations present : immediate mortality 11 (18·9%).

TABLE IX.
Schleyer's Statistics : 1. Frauenklinik, Vienna.

Remote prognosis :
  57 of 115 cases survived partial or complete surgical removal of the malignant tissue.
Five-year clinical cures :
  Carcinomatous pseudomucinous cystomata : 11 cases, 5 cures (45·4%).
  Carcinomatous papillary cystomata : 21 cases, 4 cures (19%).
  Genuine solid carcinomata : 18 cases, 3 cures (17%).
  Metastatic carcinomata : 7 cases, no cures (0%).

Miss Margaret C. Tod (_Holt Radium Institute, Manchester_): The radiotherapy of malignant disease of the ovary is discussed under five headings: (1) Types of tumour which the radiotherapist is asked to treat. (2) Results of treatment. (3) Principles of treatment. (4) Technique of treatment. (5) Tolerance of the patient towards treatment.

(1) The group of tumours discussed probably includes all the more common types and most of them have been approached as _post_-operative problems. The cases fall into four classes: (_a_) The surgeon, after removal of a tumour which has proved to be malignant, feels that a course of radiotherapy would add to the patient's safety. We do not believe that small doses of radiation have any prophylactic effect and only undertake to treat if a full course is to be given. If, therefore, we are asked to treat prophylactically

a patient in whom no sign of recurrence can be found we ask the surgeon whether he is satisfied that he removed the tumour completely and we accept the case only if he expresses uncertainty.

(b) An attempt at radical removal has been made but has failed. This group includes a few cases in which. it is known that the tumour was incompletely removed although there are clinical signs of its presence, but most of the cases do show signs of active tumour growth.

(c) A laparotomy has been performed but an inoperable tumour has been found and the abdomen has been closed, with biopsy the only procedure.

(d) A diagnosis of inoperable tumour of the ovary has been made without opening the abdomen.

The pathological findings have not given much help in deciding whether radiotherapy is called for. It would obviously be of real importance could it be determined that certain pathological types respond and others do not, but although sensitivity certainly varies and it has been thought at times that a tumour, for instance pseudomucinous cyst adenoma, was resistant there has always been the odd case which responded.

(2) In the assessment of tolerance 30 additional cases treated during 1943 are included. The methods by which the 73 cases shown in the tables have been treated have gradually evolved towards the radical technique now used in the clinic, the fields have got bigger and the dosage has increased. To conform to the rule that all cases treated must be shown they have been divided into those completely and those incompletely treated. Complete, means that large fields covering most of the abdomen were used and a planned course of therapy given. Radium in the uterus was occasionally added. "Incomplete" means either that the patient failed to finish more than half the planned course of therapy or that only palliative treatment with radium was attempted. Although radium application alone is purely palliative it is a useful supplementary treatment in those cases where the uterus is involved by the malignant process. or when there is a recurrence at the top of the vagina after the uterus has been removed with the ovarian tumour. Radium is of little use in cases where there is hæmorrhage.

TABLE I. 1932 to 1938				TABLE II. 1939 and 1940 assessed at three years				TABLE III. All cases treated in 1941 and 1942 assessed in January 1944, survival rate only from one to two years		
Method of treatment	Number treated	Alive five years	Dead		Number treated	Alive three years	Dead		Number treated	Alive January 1944	Dead
Complete	18	5*	13		9	6	3		26	13	13
Incomplete	6	0	6		9*	0	9		5	0	5

* 4 well—1 died intercurrent disease after seven years.

* Incomplete due to war conditions.

No conclusions can be drawn from these figures but in view of the short time which patients with malignant tumours of the ovary usually live after incomplete operation it is already encouraging to have 50% of the fully treated cases alive more than a year after treatment. This is not merely a survival of women whose disease has been temporarily arrested, 92% of all those alive are free from symptoms.

(3) *Principles of treatment.*—When surgery fails to extirpate a malignant tumour either because it has ruptured or because of adhesions, the entire peritoneal cavity is potentially involved. It is therefore a first principle of treatment that the whole peritoneal cavity from the floor of the pelvis to the underside of the liver must be treated. X-ray therapy of the whole abdominal cavity is sometimes described as an X-ray bath and requires very large fields.

Our first method of treatment was one which is still fairly often seen—a four field arrangement generally with fields about 15 by 10 cm. irradiating the pelvis. This method is based on an erroneous conception of the way malignant ovarian tumours grow and should be condemned. If, however, the whole peritoneal cavity must be irradiated it is clear that the biological dose which can be tolerated is unlikely to be lethal to a resistant growth. It has been pointed out that there is no safe guide to sensitivity, so all these tumours must be treated, although only a proportion of them will prove sensitive enough to respond. It is always necessary to hold the balance between volume of tissue treated and dosage, and here the nature of the growth makes volume the dominant factor.

(4) The technique of treatment.—The first method of irradiating large volumes which was evolved at the Holt Radium Institute was an arrangement of anterior and posterior parallel fields in the shape of circles 30 cm. in diameter at 60 F.S.D. The 30 cm. diameter extended from the lower border of the pubis to the xiphoid process except in unusually tall women. The disadvantages of opposing circular fields are now well known. Mayneord has shown the undesirable shape of the isodose surfaces for small opposed circles and it is possible that these disadvantages may be exaggerated as the circle increases in size.

About three years ago an effort was made to obtain more homogenous irradiation by the use of multiple fields. This meant setting up with the applicators angled away from the horizontal and, to ensure a satisfactory and constant arrangement of the fields, a simple mechanical device, the "Trunk Bridge", was brought into use. The object of this device is twofold, it allows the abdomen to be regarded as a body of regular and known shape and it allows the placing of the fields in a constant relationship to the regular body so produced.

The patient lies on her back on the baseboard centrally between the posts and with these in the plane of the centres of the oblique fields. The position of this plane on the patient is the only skin marking needed. The anterior fields are rectangles 30 by 20 cm. tilted 30° from the vertical so that they are parallel with one limb of the bridge. The central ray is in the plane of the bridge and the upper edge of the field is 2·5 cm. from the apex B. The space between the applicator and the patient is packed with bolus

FIG. 1.—Photograph of patient showing treatment with trunk bridge, packing not yet completed.
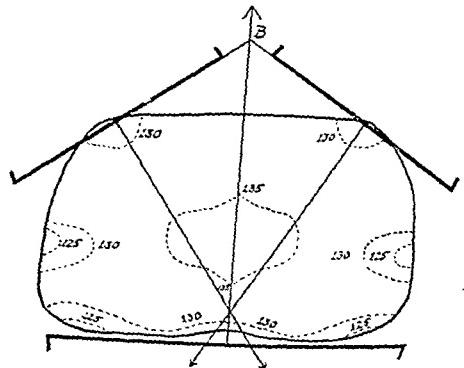
Isodose Curves for 2 Fields 30cms × 20cm and one Field 30cms ⊙

FIG. 2

bags. The posterior field is a circle of 30 cm. diameter parallel with and as close to the skin as possible. Bolus bags are again required to ensure full scattering. If the patient cannot lie on the face this field can be treated in the sitting position. When using the trunk bridge, standardization is achieved by plotting the combined isodose contours for the fields placed as described over a series of bridge heights measured from the apex to the baseboard for the anterior fields and with the applicator in contact with the skin for the posterior. The distribution of dosage is for all practical purposes homogenous on the central plane.

The prescription is given as a percentage of the given dose to each field   The dose which is described as the tumour dose, although it is delivered to the whole central zone, is 3,000 r in three to four weeks.   In treating this large volume it is necessary to begin with a low dose and increase each day until an input rate is reached which gives the desired dosage in the correct time.
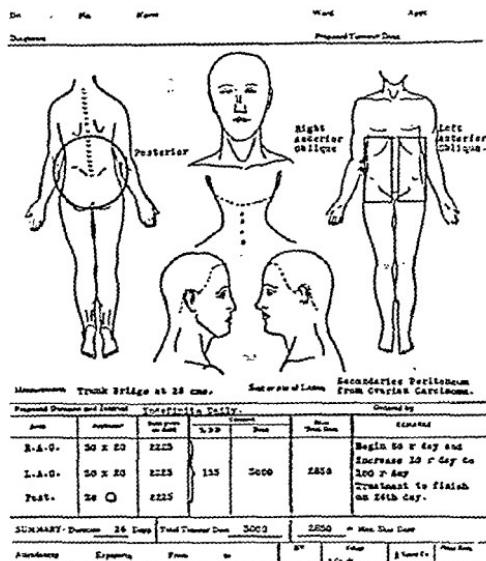
FIG. 3.—Prescription sheet for treatment of whole abdomen using trunk bridge.

(5) *Tolerance of the patient.*—It is well known that when large volumes of tissue have to be irradiated it is no longer the local tolerance of the skin and normal tissues below it which limits dosage but the general tolerance of the patient.   Intolerance manifests itself by two ways: by vomiting and diarrhœa and by a drop in the number of white cells in the circulating blood.

The first group of symptoms might be regarded to some extent as a local manifestation, an enteritis due to a radiation reaction in the gut, but the vomiting is due, in part at least, to absorption of the chemical products of irradiation.   If the graduated daily input rate, which has been referred to, is employed these symptoms are not as a rule severe enough to interfere with treatment.

The changes in the blood which follow irradiation are so constant that it is possible to use them as a guide to tolerance.   David Goodfellow published in 1935 (*B.J.R.*, vol. 8. New Series No. 96, December 1935) figures obtained from multiple counts on a series of patients treated with large quantities of radium.   Our experience with X-ray supports his contention that a fall in the lymphocyte count always precedes the fall in the polymorphonuclear leucocyte count.   He concluded that a fall in the lymphocyte count to 300 per c.c. is a danger signal even if the white count is still little below normal because it may be followed, if treatment continues, by an alarmingly sudden drop in the total count.   The figure of 300 lymphocytes must not, however, be taken as an absolute limit.   The curve, after falling rapidly to 300, may be maintained at about the same level for a period of several days or even a week while treatment continues.   The exact significance of a rising monocyte count is not yet known but it seems that there is less cause for anxiety when it also is at, or above, the 300 mark.   The total white count must also be watched and as long as it remains above 3,000 per c.c. there is no need to stop treatment.   Quite a number of the cases treated in the manner described never reach this figure, but in cases where full treatment is the patient's only chance it is reasonably safe to bring it down to 2,000 or even less, rapid recovery ensuing when treatment stops. The red count usually falls a little as does the hæmoglobin but except in cases where

there has been another cause of anæmia, such as hæmorrhage, the fall is so slight that it can be disregarded. We have not had a death directly due to effects on the blood in this series of ovarian tumours.

It is clearly desirable to relate the general tolerance as shown by the blood-count to the irradiation in terms of energy absorbed. It is now possible to get a rough assessment by using Professor Mayneord's formula for the calculation of the integral dose. His simplest formula has been used and a convention has been accepted of 10% loss in the scattering material used in packing the "trunk bridge" with an additional 5% if the patient is narrow and more side packing is required. Using this formula and convention the integral dose has been graphed against blood-counts for 34 of the cases of ovarian tumour treated with a dosage which reaches full tolerance. The integral dose is about 48 megagram roentgens in from twenty-one to twenty-four days when three fields are used. The curve at the beginning of the graph is due to a gradually increasing input rate.

FIG. 4.

FIG. 5.

FIG. 4.—Graph of integral dose in megagram roentgens against white cells in thousands per c.c.

FIG. 5.—Spot graph showing the point on the graph of integral dose at which the total white cells are reduced to one-half.

It is difficult to find a graphic method of relating the change in the white count to integral dosage. The method of choosing a definite point on the blood graph and spotting it on the graph of integral dose has been used. Integral dose varies with the size of the patient so that the "spots" are not all on one line but they come very near to it.

The first graph shows the point at which the total white count was reduced by one-half, and the second shows the point at which the lymphocyte count dropped to 300 per c.c. Both are spread over more than half the curve, the reduction to one-half total count preceding the reduction of lymphocytes to 300. The wide variation is apparently due to individual variation in the blood picture of the patients even although they are suffering from a disease which does not directly affect blood formation.

Although it is not possible to establish a direct quantitative relationship between integral dose and effect on white cells the detailed study of these cases combined with experience with a similar group of seminoma testis has established certain facts about

general tolerance. It seems that it is safe to deliver a dose of 3,000 r to the abdomen in twenty-one to twenty-four days using fields large enough to cover the whole peritoneal cavity. This involves the delivery of an integral dose of 40 to 50 megagram roentgens with the factors indicated.
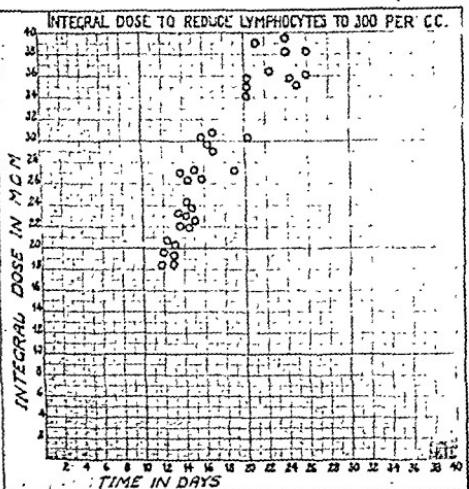
FIG. 6
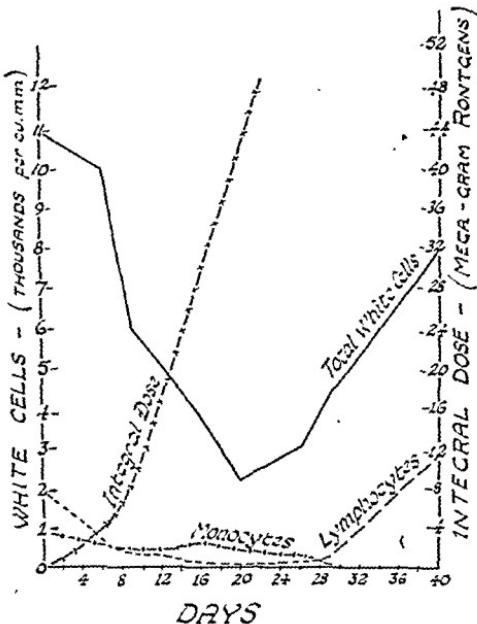
FIG. 7

FIG. 6.—Spot graph showing the point on the graph of integral dose at which the lymphocytes are reduced to 300 per c.c.

FIG. 7.—Graph of integral dose against white cells to show rapid recovery after treatment stops.

The question remains whether the biological effect of the dose of 3,000 r in twenty-four days is the best that can be obtained. The alternative would be either to obtain lethal dosage in a shorter time or to increase tolerance by lowering the input rate but continuing until a higher biological dose had been obtained. With the large volume involved the need for a gradual start rules out the short course of treatment. On the other hand, tolerance of the white cells does not seem to be sufficiently increased by prolonging time to allow a higher biological dose to be delivered to the tumour. 3,500 r in thirty days has been given from two portals but was not apparently more effective than 3,000 r in twenty-four days.

Conclusions drawn from the figures and arguments put forward are: (1) All cases of malignant neoplasm of the ovary in which removal is incomplete or impossible should have the chance of a course of X-ray therapy. (2) To obtain satisfactory results the whole abdomen must be treated. (3) A tolerable dose which can be delivered to this volume of tissue is 3,000 r in twenty-four days. (4) This dose is lethal to a fair proportion of ovarian neoplasms. (5) The systematic use of the method outlined would appreciably improve the survival rate in cancer of the ovary.

Dr. Frank Ellis (*An analysis of 105 cases of primary carcinoma of the ovary treated at the Sheffield Radium Centre* 1932 to 1939): This series of cases was referred for treatment at the Sheffield Radium Centre in the years 1932 to 1939 in co-operation with the surgeons of the Sheffield Hospitals, especially the Jessop Hospital for Women, and their help and co-operation are gratefully acknowledged.

there has been another cause of anæmia, such as hæmorrhage, the fall is so slight that it can be disregarded. We have not had a death directly due to effects on the blood in this series of ovarian tumours.

It is clearly desirable to relate the general tolerance as shown by the blood-count to the irradiation in terms of energy absorbed. It is now possible to get a rough assessment by using Professor Mayneord's formula for the calculation of the integral dose. His simplest formula has been used and a convention has been accepted of 10% loss in the scattering material used in packing the "trunk bridge" with an additional 5% if the patient is narrow and more side packing is required. Using this formula and convention the integral dose has been graphed against blood-counts for 34 of the cases of ovarian tumour treated with a dosage which reaches full tolerance. The integral dose is about 48 megagram roentgens in from twenty-one to twenty-four days when three fields are used. The curve at the beginning of the graph is due to a gradually increasing input rate.

FIG. 4.

FIG. 4.—Graph of integral dose in megagram roentgens against white cells in thousands per c.c.

FIG. 5.

FIG. 5.—Spot graph showing the point on the graph of integral dose at which the total white cells are reduced to one-half.

It is difficult to find a graphic method of relating the change in the white count to integral dosage. The method of choosing a definite point on the blood graph and spotting it on the graph of integral dose has been used. Integral dose varies with the size of the patient so that the "spots" are not all on one line but they come very near to it.

The first graph shows the point at which the total white count was reduced by one-half, and the second shows the point at which the lymphocyte count dropped to 300 per c.c. Both are spread over more than half the curve, the reduction to one-half total count preceding the reduction of lymphocytes to 300. The wide variation is apparently due to individual variation in the blood picture of the patients even although they are suffering from a disease which does not directly affect blood formation.

Although it is not possible to establish a direct quantitative relationship between integral dose and effect on white cells the detailed study of these cases combined with experience with a similar group of seminoma testis has established certain facts about

above conclusion is not changed. Analysis of figures published by Wintz [1] on 114 cases gives the same result.

Histological types.—Analysis shows a strong suggestion that the malignant pseudo-mucinous cyst with 80% surviving more than three years has a much better prognosis than the papillary adenocarcinoma with 36% surviving more than three years.

Prognosis of unilateral and bilateral ovarian involvement.—This comparison showed that 20 out of 40 (=50%) of cases with one ovary affected survived for three years or more while 10 out of 36 (=24%) of the bilateral tumours survived. Analysis shows that this is a significant difference so that the conclusion may be drawn that the prognosis is significantly worse if both ovaries are affected.

Comparison of completely operated with incompletely or non-operated cases.—Of the cases treated, as is expected, those in which a complete removal can be carried out are shown to have a much better prognosis, 17 out of 25 (=68%) surviving more than three years as compared with 11 out of 51 (=22%). All these were treated cases. The probability that this could be due to chance proves on analysis to be less than 1:1,000 so that the possibility of a complete operation is proved to be associated with a better prognosis. Wintz's figures, analysed from the same point of view, do not, however, show a significant difference in prognosis although the corresponding percentages are 78% and 41%.

Effect of delay in referring cases for radiotherapy.—Only completely operated cases with no gross disease at the time of irradiation were considered. In these cases it appears that with a gap of one month or less after the operation 8 cases out of 8 survived more than three years while of the others 6 out of 10 survived. The difference between 100% and 60% survivals is not significant and might be due to chance with these figures the probability being 1/10—1/5 that this is so. Nevertheless, though not proved the figures are suggestive that delay after operation in beginning radiation worsens the prognosis.

The effect of method of treatment on survival.—Figures published by Schroeder [2] indicated that radium combined with X-ray treatment improves the prognosis.

(*a*) *Cases which died before three years compared with those living after three years.*—Of the cases treated with X-rays, 7 out of 20 (=35%) survived more than three years, while those treated with both radium and X-rays show a survival of 15 out of 34 (=44%). The probability that this difference could be due to chance is greater than 1:2 so that this comparison shows no significant difference between the two methods of treatment in their influence on survival.

A comparison using a different test and taking account of the survival in months of each case after treatment was made, showed that the mean survival in the case of the combined treatment was 18·3 months and for the cases treated by X-rays only was 8·5 months. The standard deviations were large (X+R 17·77 months X−6·48 months) but the standard error of differences between the means was found and divided into the differences between the means. The resultant value of "t" was 1·907 which for 33 degrees of freedom (35 cases) gives a probability of only 1:16 that the longer survival was due to chance. Thus the suggestion is strong that the fact that the cases treated with radium +X-rays survived longer than those treated by X-rays only is significant although it is not proved to be significant.

(*b*) *Cases with definite disease at the time of treatment. X-ray treatment only compared with radium + X-ray treatment.*—Of these cases treated with X-rays only 2 out of 20 (=10%) survived more than three years while of those treated by the combined agents 9 out of 32 (=28%) survived. These percentages seem significant but analysis shows that the possibility is between 1/5 and 1/10 that this result could be due to chance. Therefore the result cannot be considered statistically significant.

(*c*) *Cases with no disease at the time of radiation.*—Of these cases treated with radium + X-rays, 9 out of 9 survived more than three years (=100%). Of those treated with X-rays only 5 out of 8 (=63%) survived for the same period. This difference proves on analysis to have a probability of 1/16 only that it is due to chance. *While not statistically acceptable as proof it gives a strong suggestion that X-ray + radium treatment offers a significantly better prognosis than X-ray treatment only.*

Influence of X-ray technique on results.—Several techniques were used during the period under review. Analysis showed no significant difference in the effects of the

The series is of the same order of size as almost any that has been published in co[...] nexion with radiotherapy but statistical analysis shows that the sub-groups are too sm[...] to allow of unequivocal conclusions to be drawn. This is no reflexion on the series [...] cases but serves to show that other series, if subjected to the same type of analysis, woul[...] be equally or more inconclusive. The results are summarized in the following tables:

TABLE I.—PRIMARY OVARIAN NEOPLASM.
Cases referred 1932-1939, Sheffield Radium Centre.

Year	No.	Alive (when traced)	Dead
1932	1	0	1
1933	3	1	2
1934	10	3	7
1935	23	6	17
1936	23	6	17
1937	22	5	17
1938	11	1	10
1939	12	4	8
Totals	105	26 / 25%	79 / 75%

TABLE II.—CASES ALIVE.

Year	With disease	Without disease	Doubtful histology	Untraced less than 3 years
1932	0	0		0
1933	1	0		0
1934	1	0		0
1935	1	2	1	0
1936	1	4	1	1
1937	0	5	2	0
1938	0	5	1	0
1939	1	3		0
	5	20	5	1

After three years   30 = 28.6%   Alive with disease 9 = 8.6% of 105   Alive without disease 21 = 20.0% of 105 }28.6%

After five years   26 = 24.8%   Alive with disease 7 = 6.7% of 105   Alive without disease 19 = 18.1% of 105 }24.8%

The type of case referred.—Statistical analysis shows that cases in which a complete removal was carried out were mostly referred for treatment with recurrence after two months and without recurrence before two months after the operation. (Before two months 15 without and 3 with recurrence. After two months 4 without and 13 with recurrence.) For these figures the probability that the difference is due to chance is less than 1/100 and therefore it must be concluded that while some cases were referred for treatment as a routine, many were referred only after recurrence.

The value of radiotherapy.—To assess the value of radiotherapy in treating carcinoma of the ovary it was necessary to analyse only cases with definite recurrence or residue at the time of treatment because while cases with no obvious disease were treated, no cases with no obvious disease were not treated so that the treated and untreated cases in this series are not comparable unless definite recurrence or residue was present at the time of treatment.

CASES WITH DEFINITE RECURRENCE OR RESIDUE.

Untreated	Surviving more than 1 year	... ...	5 = 25%
	Surviving less than 1 year	... ...	15 = 75%
Treated	Surviving more than 1 year	... ...	30 = 44%
	Surviving less than 1 year	... ...	38 = 56%

The differences of the percentage figures seem definite but a statistical test shows that the possibility that this result could be due to chance is between 1/5 and 1/10 so that the figures are not statistically significant. *It is not proved that treatment is really helpful but it is strongly suggested that it is.*

For similar figures for three-year survivals the percentages are even more striking, 5% of the untreated and 22% of the treated cases surviving. A similar analysis, however, gives about the same probability that the results could be due to chance so that the

above conclusion is not changed. Analysis of figures published by Wintz [1] on 114 cases gives the same result.

Histological types.—Analysis shows a strong suggestion that the malignant pseudo-mucinous cyst with 80% surviving more than three years has a much better prognosis than the papillary adenocarcinoma with 36% surviving more than three years.

Prognosis of unilateral and bilateral ovarian involvement.—This comparison showed that 20 out of 40 (=50%) of cases with one ovary affected survived for three years or more while 10 out of 36 (=24%) of the bilateral tumours survived. Analysis shows that this is a significant difference so that the conclusion may be drawn that the prognosis is significantly worse if both ovaries are affected.

Comparison of completely operated with incompletely or non-operated cases.—Of the cases treated, as is expected, those in which a complete removal can, be carried out are shown to have a much better prognosis, 17 out of 25 (=68%) surviving more than three years as compared with 11 out of 51 (=22%). All these were treated cases. The probability that this could be due to chance proves on analysis to be less than 1 : 1,000 so that the possibility of a complete operation is proved to be associated with a better prognosis. Wintz's figures, analysed from the same point of view, do not, however, show a significant difference in prognosis although the corresponding percentages are 78% and 41%.

Effect of delay in referring cases for radiotherapy.—Only completely operated cases with no gross disease at the time of irradiation were considered. In these cases it appears that with a gap of one month or less after the operation 8 cases out of 8 survived more than three years while of the others 6 out of 10 survived. The difference between 100% and 60% survivals is not significant and might be due to chance with these figures the probability being 1/10—1/5 that this is so. Nevertheless, though not proved the figures are suggestive that delay after operation in beginning radiation worsens the prognosis.

The effect of method of treatment on survival.—Figures published by Schroeder [2] indicated that radium combined with X-ray treatment improves the prognosis.

(a) *Cases which died before three years compared with those living after three years.*—Of the cases treated with X-rays, 7 out of 20 (=35%) survived more than three years, while those treated with both radium and X-rays show a survival of 15 out of 34 (=44%). The probability that this difference could be due to chance is greater than 1 : 2 so that this comparison shows no significant difference between the two methods of treatment in their influence on survival.

A comparison using a different test and taking account of the survival in months of each case after treatment was made, showed that the mean survival in the case of the combined treatment was 18·3 months and for the cases treated by X-rays only was 8·5 months. The standard deviations were large (X+R 17·77 months X−6·48 months) but the standard error of differences between the means was found and divided into the differences between the means. The resultant value of "t" was 1·907 which for 33 degrees of freedom (35 cases) gives a probability of only 1 : 16 that the longer survival was due to chance. Thus the suggestion is strong that the fact that the cases treated with radium +X-rays survived longer than those treated by X-rays only is significant although it is not proved to be significant.

(b) *Cases with definite disease at the time of treatment. X-ray treatment only compared with radium + X-ray treatment.*—Of these cases treated with X-rays only 2 out of 20 (=10%) survived more than three years while of those treated by the combined agents 9 out of 32 (=28%) survived. These percentages seem significant but analysis shows that the possibility is between 1/5 and 1/10 that this result could be due to chance. Therefore the result cannot be considered statistically significant.

(c) *Cases with no disease at the time of radiation.*—Of these cases treated with radium + X-rays, 9 out of 9 survived more than three years (=100%). Of those treated with X-rays only 5 out of 8 (=63%) survived for the same period. This difference proves on analysis to have a probability of 1/16 only that it is due to chance. *While not statistically acceptable as proof it gives a strong suggestion that X-ray + radium treatment offers a significantly better prognosis than X-ray treatment only.*

Influence of X-ray technique on results.—Several techniques were used during the period under review. Analysis showed no significant difference in the effects of the

methods used. In the case of one method, the combination with radium treatment gave an average survival of 22·57 months in the cases which had died while with that of X-ray treatment only the average survival was only seven months. Despite the great difference analysis showed that such a result had a probability between 1/5 and 1/10 of being due to chance.

Influence of dose of radiation on survival.—This comparison was difficult because of the uncertainty of combining radium with X-ray dosage. The value of the comparison, however, justifies an approximation and using the isodose curves for the radium treatment used it appears that 2,000 r at the pelvic wall may be added to the X-ray dose for three Stockholm treatments (7,920 mg.hrs.) with radium and proportional dose in roentgen for one and two applications of radium.

When this was done the following table emerged:

Dead Cases after Radiation.

Dose	No. of cases	Mean survival
< 500 r	19	6·3 months
500 r – 2,500	17	9·94 months
2,500 – 4,500	20	9·8 months
4,500 – 6,500	11	24·2 months

Further subdivision produced the following table:

Dose	Mean survival
3,600 – 4,000	7·3 months
4,000 – 4,500	14·3 months
4,500 – 6,500	24·2 months

These figures appear to show definitely that the larger the dose the better the survival. Again, however, the results prove on analysis not to be significant statistically, the probability that they can be due to chance being between 2/10 and 3/10. Thus, although such figures would be accepted by most doctors as having a definite significance, this contention would be disputed very vigorously by the statisticians.

We are thus faced with the conclusions, in addition to those made in the foregoing discussion, that even though a relatively large series of cases has been analysed the definite conclusions which can justifiably be drawn, from the point of view of a statistician, are scanty. Bearing in mind that such series of cases are uncommon it seems that if such work could be carried out by hospitals acting in co-operation with a view to providing the answers to certain questions, those answers are more likely to be provided because one feels that only the smallness of the groups in the above series prevents them from providing significant statistical evidence on the points at issue.

REFERENCES

1 WINTZ, H. (1932) *Strahlentherapie,* 44, 211.
2 SCHROEDER, C. (1934) *Strahlentherapie,* 51, 465.

Mr. T. Anthony Green: I am surprised that such a large volume of tissue as the whole abdomen and pelvis is radiated *en bloc* to a dosage of at least 3,000 r by the Manchester School. Calculation shows that a skin dose of 200 r per day would give a body dose of one megagram roentgen daily. An average figure for most treatments does not exceed half a megagram roentgen daily.

My experience has been that patients of any size are ill after such a large body dosage and it has often been found beneficial to treat the patient in stages, i.e. pelvis first and abdomen later or up in strips. This spreads out the body dosage over a longer time. but does not increase the overall treatment time for each block of tissue treated.

Secondly in treating ovarian tumours an interesting and important fact should be remembered—that is the mobility of pelvic structures. By means of localizing a metallic body in the vaginal vault, I have been able to demonstrate that in certain patients as much as 5 cm. movement occurs when changing from the dorsal to the ventral position. As nearly all treatments are given from above, this means the dosage may be reduced by the diseased area falling away. Whenever possible it would therefore seem to be an advantage to treat from below.

Miss Tod (in reply): We have treated a large number of patients in the manner described and we have never had any serious trouble due to the large volume of tissue irradiated.

DISCUSSION ON ADVANCED CASES OF CARCINOMA OF THE BREAST TREATED BY STILBŒSTROL

Dr. Frank Ellis, in opening the Discussion, said that the following points should be considered :

(1) Whether any effect is produced on the course of carcinoma of the breast by stilbœstrol.

(2) Whether age of patient or menopause exerts any influence on this effect.

(3) Whether the response is affected by the histological and cytological structure of the tumour.

(4) The dosage, including maintenance dose, if any.

(5) The symptoms associated with its administration and the contra-indications to its use.

(6) Possible changes in the serum acid and alkaline phosphatase such as are associated with improvement in carcinoma of the prostate.

Dr. Ellis reported on 21 cases of carcinoma of the breast in which the stilbœstrol effects were observed with no complicating influence of radiation. The dosage was relatively heavy—about 15 mg. daily. 3 cases showed complete intolerance to stilbœstrol. The youngest was 35 years of age and the oldest 81. The average age of the 4 who improved on stilbœstrol was 64·2. 1 case was that of a male aged 69 with abdominal gland involvement. He received 15 mg. daily for three months. His symptoms were unchanged.

In all cases the chief symptoms were nausea, vomiting, activity of the breasts with tenderness, swelling and pigmentation of the areola, resumption of menstruation in a few cases (so severe in one case as to necessitate a blood transfusion) and œdema of the ankles. Of these the nausea and vomiting was always immediate, the others being delayed two to six months.

There was also in the cases which improved a definite feeling of well-being with a remarkable increase of appetite. Progress was assessed where possible by measurements. No phosphatase estimations could be carried out.

Dr. S. Bryan Adams said that his series were all at an advanced stage for which other treatment was not available or not indicated. They represented a complete series and a selection had not been made in view of the results obtained.

The dosage varied from 1 to 15 mg. daily, the first case receiving only 1 mg. daily showed such a marked improvement that the dosage was not increased.

The oldest patient was 82 and the youngest 36. The average age was 62·3.

The woman of 82 had nodular recurrences in left breast following a local excision four years previously. After two months of stilbœstrol treatment (5 mg. t.i.d.) she showed marked improvement and no nodules were palpable.

Mr. G. W. Blomfield: 10 cases were treated at Sheffield, with doses varying from 2 mg. to 15 mg. per day. Some had nausea on small doses or large doses. Some were disturbed by the physiological actions of the drug when "menstruation" commenced again after the menopause. As a whole the side effects were not excessive and patients did not object to taking the drug when an explanation was given.

Accurate assessment of the size and extent of the tumours was attempted. In some cases histological sections were taken after treatment to determine whether the mitotic activity and microscopic appearance was affected.

There were 5 cases only where the growth could be accurately measured and where 10 mg. or more was given daily. No definite evidence of growth control could be found in these cases.

No striking results were met with in this series. It was interesting to note that ulceration of one growth healed up and the size of the tumours remained constant. Histological sections, however, showed no evidence of control; the cells were unaffected and mitoses were numerous.

Dr. Alexander Haddow (*Chester Beatty Research Institute, Royal Cancer Hospital* (*Free*)): This communication deals with 13 cases of advanced cancer of the breast. Many of these had previously received treatment by surgery, and showed recurrence, or had been treated by high voltage therapy, although a sufficient interval had elapsed since such treatment to make any confusing effect improbable.

Stilbœstrol was given in total doses varying from 75 mg. to 676 mg. over periods of treatment varying from four weeks to twenty-four weeks; the average total dose being about 350 mg. in an average treatment period of over eleven weeks. Administration was by mouth, or by intramuscular injection, and in some cases by both routes.

In cases showing some degree of response which could reasonably be attributed to the drug, the sequence of changes was characteristic. Lesions previously red in colour tended to develop a purplish discoloration or sometimes pallor, small skin nodules would show scabbing, or flattening, and occasionally disappeared, and larger nodules and masses might undergo partial regression. Dr. Haddow showed 2 tables of which the following is a summary:

Table I showed a classification of the response in these 13 cases, divided into three categories. In Group A (9 cases) the disease showed uninterrupted progress, being apparently quite unaffected except possibly to a very minor degree in 2 cases. In Group B, consisting of 3 cases, the disease also continued to advance, but after a short period in which the breast tumour showed some retardation of growth, or partial regression, almost certainly attributable to treatment. Only the single remaining case manifested a marked and more lasting change, which has continued to the present date over a period of four months, and which consisted of a considerable degree of regression affecting both the primary tumour and secondary deposits in the axillary lymph nodes.

Table II showed the details of age, total dosage, and duration of treatment in the three classes. Age in Group A, that is in those patients showing little or no favourable response, varied from thirty-one years to sixty-eight years. The mean age in Groups B and C together, that is those showing a *temporarily favourable* or *markedly favourable* response, is considerably higher than in Group A, 62 as against 48, that is a difference of fourteen years. The numbers are of course very small, and no real conclusion can be drawn, but it may be of interest that the difference in age between those showing no response, and those showing some favourable response, is statistically significant. This is mentioned merely as a suggestion that favourable response may possibly be more likely in older and post-menopausal age-groups, and as an indication of the need for very much larger numbers before positive conclusions can be drawn.

Total dosage is essentially comparable in the different groups. *Duration of treatment* is somewhat longer in those cases showing favourable response. This is perhaps not a significant feature, as experience has shown that response, where it occurs, has been evinced at an early stage (between one and two months) after the commencement of treatment.

FIG. 1.—Carcinoma of the breast. The local condition in the case showing most favourable response: (A) at 7.2.44 (immediately before treatment); (B) at 22.5.44.

Fig. 1 gives a comparison of the local lesion in the most favourable case, at an interval of fifteen weeks. In this case—a spheroidal-cell carcinoma—a lump in the breast was noticed by the patient in 1942, and it so happens this is the only case of the series which had not received any form of treatment previously.

Two points will be noted: (1) The pronounced regression of the primary tumour, and (2) the areolar pigmentation due to the administered œstrogen. In this case partial regression also occurred in a secondary mass in the axilla.

Examples of this kind, however exceptional, are of course both clinically striking and of the greatest fundamental importance. It should clearly be one of the purposes of an investigation such as this, which is only in its preliminary stages, to attempt to determine whether these highly favourable cases are simply the exceptional responses which may be encountered in a uniform population, or whether they represent a special type of breast cancer: that is, whether breast cancer, in its relation to stilbœstrol, represents a unity, or comprises several different categories. This is information which can only be obtained from the investigation of comparatively large numbers.

If cancer of the breast is homogeneous, the relation may be (1) that the great majority of cases show little response; (2) that most cases show a medium degree of response and only small numbers show either no response or a marked response; (3) an intermediate type where more cases show some response than no response. If, on the other hand, cancer of the breast (in this respect) comprises several categories, the distribution of responsive cases may be a composite one. To obtain this knowledge would require, as well as large numbers, a *measure* of response, as by some system of clinical assessment or marking. This in turn would involve close contact between the various collaborators, so that their clinical criteria might be as uniform as possible. It is comparatively easy to classify the least responsive and the most responsive cases: the main difficulty would arise from the classification of intermediate groups with medium degrees of response.

Response may possibly be correlated with any one, or several, of a large number of factors, such as age (which has already been discussed in a tentative way), dosage, duration of treatment, menstrual and reproductive history, and so on. The present series is too small to allow any correlation with the histological or cytological nature of the tumour, yet this is another obvious factor of likely importance. A further possibility is that the metabolism of the œstrogen may be different in different cases.

Dr. W. M. Levitt reported on 11 cases. 7 treated at St. George's and 4 at St. Bartholomew's Hospital. All were advanced carcinoma of the breast, 7 had multiple skin and subcutaneous deposits, 3 had bone deposits and 1 chest deposits. The general condition was good in 7 cases in the series and fairly good in the remainder. Dosage was standardized commencing with 2·5 mg. of stilbœstrol three times a day and working up rapidly to 5 mg. three times a day, at which level the dosage was maintained until death or the present time. In only 1 case was improvement noted. This was a woman of 69 with a fungating ulcer. This ulcer became much cleaner and reduced in area from 66 sq. cm. to 20 sq. cm. The improvement has been maintained for four months although disease is still present. This was the only patient over 60 in the series. None of the others was improved and 5 are dead.

Dr. R. McWhirter: Up to May 1944 37 cases of carcinoma of the breast were treated with stilbœstrol. All the patients had advanced disease. The dosage given was 5 mg. twice a day.

Of the 37 cases treated 6 showed very definite improvement. In the remainder the progress of the disease was not affected beneficially and indeed in 2 cases the patients appeared to have been made worse by the treatment.

All 6 patients in whom definite improvement occurred were over 50. The average age was 62 years and the youngest was 52 years.

The histological type was known in 4 and in all 4 the tumour was undifferentiated. On the other hand of the 2 cases apparently made worse by stilbœstrol the histological type was known in one and the tumour was well differentiated.

The improvement may not be maintained even when the stilbœstrol is continued. In the first and third cases some deterioration has taken place.

Apart from the effects noted on the tumour tissue the only point calling for comment is that with the level of dosage used patients were rarely upset by the treatment. Only 1 patient was unable to continue the treatment on account of sickness. More recently, by the courtesy of Messrs. Glaxo, dienœstrol has been used and of the patients so treated none has suffered from sickness. Dienœstrol is more potent than stilbœstrol and 1 mg. of the former is equivalent to 3 to 5 mg. of stilbœstrol.

Dr. Edith Paterson reported on 13 patients treated with stilbœstrol and also on a group of 23 patients treated with triphenylchloroethylene. All were advanced cases of breast carcinoma, and no case had had recent radiation treatment.

She said that triphenylchloroethylene, like stilbœstrol, was a synthetic substance with the pharmacological action of the natural follicular hormone of the ovary. Experience showed that the effect on the breast and also the side reactions on the patient were similar with the two drugs.

Patients receiving either drug were classified as to whether their tumours showed measurable regression even if slight and temporary, whether their tumours remained stationary or whether the disease progressed during treatment. [Stationary and progressed cases are under "Not Improved" in table.]

In the cases treated by stilbœstrol a biopsy was obtained in all cases.

In the 2 regressing cases a reduction in size of the tumour occurred and a considerable degree of epithelialization of the ulcer. No local treatment was used in these cases.

With stilbœstrol the average length of treatment was 12·2 weeks and the average daily dose was 5·8 mg. The average age was 56·2 years. With trichloroethylene the overall period of treatment and observation was longer and the doses of œstrogen were larger than in the stilbœstrol series. In over half the cases a biopsy was obtained. With triphenylchloroethylene the average length of treatment was twenty-seven weeks; the average daily dose was 3 g. The average age was 55·6 years.

Regression following either of the drugs was most marked in the established primary mass whether this was the original breast tumour or recurrent nodules on the chest wall. Bone metastases were also sensitive either regressing or ceasing to give pain (4 cases).

Secondary deposits in lymph nodes seemed on the whole less sensitive and it was commonly observed that the original lesion could be regressing while fresh foci appeared in lymph nodes or in the opposite breast, or in the lungs.

Regression when it occurred could not be correlated with the size of the dose of either drug within the limits of dosage used. Nor was it associated with the length of time of treatment; cases which showed regression did so within a few weeks of the commencement of treatment. It is interesting that regression occurred in the only male case in the group.

Only one positive correlation was found. The pathological characteristics of tumours seemed related to the effects observed in that the more cellular tumours were the most responsive. No scirrhous tumour in either group showed any response and of the tumours actively progressing during treatment, the majority were scirrhous in type. The greater effect in the non-scirrhous type may be dependent on the greater vascularity of the tumour so that the drug can more easily reach the malignant cells.

Neither drug would seem to have a curative value and neither is as effective or certain in its results as palliative X-ray therapy. The findings, however, are of scientific importance and should encourage an extended trial of other allied substances.

Slides were shown illustrating the degree of regression in 3 cases and illustrating the histological changes in one tumour following treatment.

Dr. C. J. L. Thurgar: The 10 cases of carcinoma of the breast treated with stilbœstrol here reported are taken from a larger series of nearly 30 patients who have received the drug. The 10 are consecutive cases who have received a dosage of not less than 10 mg. a day, patients who could not tolerate this amount having been excluded. The results obtained approximate closely to those in the series as a whole. The average age was 58·6. The youngest was 38 and the oldest 76.

Those cases which give a definite result appear to respond immediately and steadily. Objective improvement is apparent within one month of treatment by stilbœstrol.

The 10 cases above include 5 in whom stilbœstrol exerted no influence on the natural course of the disease. 5 showed some improvement and these comprised: 1 (aged 58) rapid and spectacular response, 2 cases of definite and continued general and local improvement and 2 who were subjectively improved, but in whom the objective response was transient.

Of the possible factors involved, age seems to be the most important consideration. I have not observed any patient under the age of 58 who has shown any objective improvement to stilbœstrol therapy and the majority of the patients who have shown any response have been well over 60. It may well be that those conditions which bring about regression of breast cancer on the administration of œstrogens depend upon the establishment of a balance in the ductless gland system which is only reached some years after the menopause.

The influence of dosage seems more difficult to determine. Though most of the earlier cases in my series were given 10 mg. or more daily, other patients, who were put on stilbœstrol by their family doctors before being brought to my notice, include several who manifested great improvement on very small dosage levels.

Other broad impressions which emerge are that little hope can be entertained from stilbœstrol therapy for patients who are in very poor general condition or for those who have large recurrences in areas that have been irradiated to the limit of tolerance, though I have seen individual cases which refuted each of these generalizations. One puzzling

feature shown by a number of cases is the varying degree of response of different metastases in the same patient. Some deposits may even regress, while others enlarge or new ones appear.

In assessing the results of stilbœstrol treatment, it must be borne in mind that breast cancer is a form of malignant disease which sometimes shows spontaneous remissions or even regressions, though these are probably always temporary.

Dr. James Z. Walker (*Radiotherapy Centre, County of Lincoln*): The survey by Harvey and Dawson has indicated that the incidence of malignancy in all breast tumours became very high as the 40 to 60 age-period was reached. The following graph could be drawn from their figures (A) and (B):
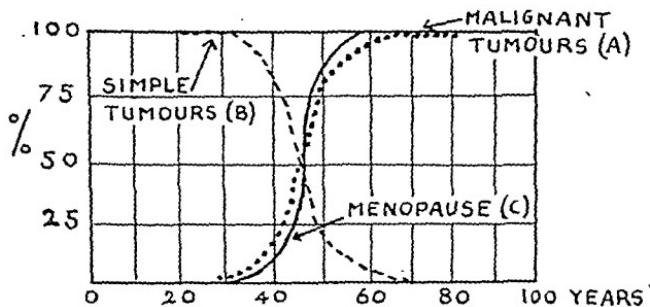
If the graph for the age-period at which the menopause develops is added, then curve "C" can be drawn. The striking proximity of curve "A" and curve "C" is remarkable.

The cycle of events (climacterium) which brings about the menopause may last many years; the cessation of menstruation is only a small arc in this cycle.

The onset of the climacterium would appear to be associated with either an atrophy or a dysfunction of the ovaries with the secretion of abnormal hormones (cp. thyrotoxicosis), which may result in a metropathia hæmorrhagica or other pathological process in the ovaries or uterus, &c., and/or alternatively, this derangement or loss of normal ovarian function may bring about an alteration in the cellular activity of breast tissue which results in a mastopathia (so-called chronic mastitis, &c., all belong to this group of conditions). With the cessation of the menses, the ovarian œstrogenic hormones do not immediately disappear from the blood and urine, but do so in 80% of women within three years, about half of the remaining 20% do so subsequently and the rest perhaps not at all.

The atrophy of the ovaries may be associated with an over-secretion (or a failure of utilization, or neutralization) of the gonadotrophic hormones of anterior pitpuitary origin (i.e. follicular maturation hormone, luteogenic hormone and prolactin). In this way, an imbalance develops between the various endocrine glands, resulting in a thyroid hypoactivity and probably a hyperactivity of the suprarenal cortex. This manifestation would seem to account for the vasomotor and blood-pressure disturbances of the climacterium. Metabolic activity of tissue cells becomes altered, gross manifestations of which show themselves as glycosuria, increased adiposity, &c.

From the foregoing it can be expected that the cellular activity of the breast, losing the control of ovarian (normal) œstrogenic chemical substances, becomes abnormal and pathological, and, in certain areas, frank malignancy develops.

In the attempt to counter this process, it has been thought that by giving large doses of one of the ovarian œstrogenic substances (e.g. diethyl stilbœstrol), one could restore this normal balance between anterior pituitary, thyroid, suprarenal, and ovarian hormones, and, by so doing, either destroy breast malignancy or, alternatively, set up a state of affairs in which breast cancer cells are incapable of survival. If cancer of the breast is due to a chemically abnormal substance, either produced by ovary or anterior pituitary (or elsewhere), the saturation of the body with a normal ovarian hormone will either neutralize this substance or, by virtue of its concentration, prevent it from acting on mammary tissue.

One line of attack on the problem is to assume that cancer of the breast is due to ovarian activity (normal or pathological) and that castration is of considerable benefit

in the control of the disease. The other is that it is the loss of ovarian function that allows endocrine substances of non-ovarian origin to have unrestrained action on breast tissue.

On this second assumption, the purpose of this test is based: 10 cases of breast cancer were chosen, and notes made on how they have responded to daily doses of diethyl stilbœstrol.

The dosage varied from 1-2 mg. t.i.d. to 10 mg. t.i.d. This latter dose was well tolerated in a woman aged 64 with involvement of both breasts and axillæ.

There was no complete cure in the 10 cases. The average age of the 3 who were considerably improved was 67·3 years. The treatment was of no value in 5 cases, whilst in 2 cases there was an adverse effect. In the case of carcinoma of male breast (aged 71) the effect of the stilbœstrol was to cause increased cellular activity of the breast cancer.

Professor B. W. Windeyer: My 10 cases were all cases of advanced carcinoma of the breast. 2 of them had had no previous therapy. The remainder had all had previous treatment, surgical removal in 5 cases and X-ray therapy to the primary lesion or to recurrences or metastases in 7 cases. Skeletal metastases were present in 3 cases. Pleural effusion was present in 2. They are, therefore, a series of very advanced cases.

The period of observation was on the average of five months' duration.

Of the 10 cases, 3 showed demonstrable improvement.

In none of the 10 cases has there been complete clinical disappearance of the growth, but 3 have improved.

In 4 cases no improvement has been noted and the disease has extended.

In the final 3 cases there has been no demonstrable clinical change since treatment was started. It is possible that there has been some retardation of the growth.

Stilbœstrol would appear to have had some effect in causing regression or retardation of growth. Its action, however, is uncertain and it has not caused complete disappearance of the disease in any case.

Professor E. C. Dodds: Stilbœstrol was produced as a substitute for œstrone and œstradiol and for experimental work of academic interest on the specificity of the œstrogenic reaction. It fulfilled all these expectations, and in addition it was found to control the symptoms of carcinoma of the prostate. If it has any action on cancer of the breast, this must be regarded as a kind of "pourboire". I am surprised that the doses given have not been much heavier in an attempt to evaluate whether the failure in a number of cases is due to a lack of sensitivity to the drug. It would also be interesting to try the other two synthetic œstrogens, namely hexœstrol and dienœstrol. The latter is a more powerful œstrogenic substance when administered by mouth. The definite improvement in a number of cases in women of menopausal and post-menopausal age requires very careful reviewing. The general systemic effect of œstrogens in the menopause is very striking and there is an immediate improvement in the woman's general condition and particularly a feeling of well-being. This must be allowed for. Finally, if the very excellent suggestion made by the Chairman is carried out—namely that the work should be continued—would it not be advisable to perform a rigid series of controls?

STILBŒSTROL CASES.

	Under 60				60 and upwards			
	No.	Improved	Not improved	Spectacular improvement	No.	Improved	Not improved	Spectacular improvement
Dr. S. Bryan Adams	4	1	3	—	6	3	3	1
Dr. R. McWhirter	20	3	17	—	17	3	14	1
Dr. J. Z. Walker	4	—	4	—	6	3	3*	—
Dr. C. J. L. Thurgar	5	1	4	1	5	4	1	—
Dr. W. M. Levitt	10	—	10	—	1	1	—	—
Prof. B. W. Windeyer	8	3	5	—	2	—	2	—
Dr. F. Ellis	13	—	13	—	8	4	4*	2
Dr. Edith Paterson Stilbœstrol	8	—	8	—	5	2	3	—
Triphenylchloroethylene	13	5*	8	—	10	4	6	—
Mr. G. W. Blomfield	7	—	7	—	3	—	3	—
Dr. A. Haddow	8	1	7	—	5	3	2	1
	100	14	86	1	68	27	41	3

Under spectacular improvement are classified cases of which the following are typical : Ellis, Cases V. and VII. The breast tumour rapidly disappeared in both cases. The affected axillary glands also disappeared in Case V. In Case VII the axillary mass was reduced to one-fifth of its size.

* One male breast.

Section of Otology

President—T. B. Jobson, M.D.

[*March 3, 1944*]

Surgical Treatment of Otosclerosis

By I. Simson Hall, F.R.C.S.E.

That hearing can be improved by making an artificial opening into the labyrinth has been known since 1876, when Kessel first demonstrated the fact.

The main object of the surgeon since that time has been to replace the immobilized stapes by a movable membrane. Whether this is justified as the main aim is still open to proof, but the fact remains that mobilizing the fluid within the labyrinth results in an immediate and most dramatic improvement in hearing.

This may be accomplished in a variety of ways. It may be carried out with a small-sized mastoid gouge, used as a scraper, and a small hand lens, giving almost negligible magnification, or it may be carried out with elaborate equipment which is commonly used now. It is interesting to recall that one of my most successful fenestrations was done with the aid of the simpler equipment.

The technique for my earliest operations was very similar to that which I employ to-day, but without the specialized equipment. It is significant that improvement in results has kept pace with advance in technique.

Following Sourdille's advice I tried doing the operation in multiple stages, and experimented with cases using one to three stages. I came to the conclusion that there was no advantage in my hands of prolonging treatment, and I settled down to carry out the operation in one stage.

The position of the fenestra has also been the subject of some experiment. It has been placed in the canal itself following Holmgren's ideas. The same position was tried using Sourdille's technique. Then for a series of cases, a position over the ampulla was used. Again a reversion to the original technique was made, placing the fenestra over the ampulla, and that is the method used in the latest series.

A series of cases was also operated upon using the roof of the vestibule as advocated by Lempert, but, possibly by chance, this series was found to give inferior results, and the opening was taken more posteriorly to its former position. Perseverance with Lempert's position of the opening might have been found to give results similar to that obtained in the other methods, but the method used now is the easiest technique of all.

Approach to the middle ear is made through a post-aural incision or an end-aural incision. It does not matter which route is used provided that the operator is familiar with the method. I used the end-aural route in mastoid operations a sufficient number of times to make my operating time the same as when using the post-auricular route, which I take to mean that facility with either route was equal. Having reached this point, I decided that the post-auricular route was superior.

Anæsthesia

The ideal anæsthetic for this operation is one which gives a slight degree of anæsthesia, lowers the blood-pressure, and is safe to use over a prolonged period. This anæsthetic has, unfortunately, not yet made its appearance. Local anæsthesia permits testing of the hearing on the operating table and gives a bloodless field. Pre-medication, with hyoscine and omnopon, is of great assistance, and I have tried avertin and other basal narcotics. A method I found very effective was to use local anæsthesia up to the opening of the labyrinth and when the patient became distressed, as is usual at this point, to give pentothal intravenously for as long as necessary.

At present a heavy pre-medication followed by light ether is the method used, and this is satisfactory on the whole as I have found that the delay caused by bleeding is more than compensated by the immobility of the patient and the greater speed which can be achieved under general anæsthesia. The small movements of the patient which occasionally take place under local anæsthesia are annoying when using the microscope, and general anæsthesia eliminates these.

Oct.—Otol. 1

in the control of the disease. The other is that it is the loss of ovarian function that allows endocrine substances of non-ovarian origin to have unrestrained action on breast tissue.

On this second assumption, the purpose of this test is based: 10 cases of breast cancer were chosen, and notes made on how they have responded to daily doses of diethyl stilbœstrol.

The dosage varied from 1-2 mg. t.i.d. to 10 mg. t.i.d. This latter dose was well tolerated in a woman aged 64 with involvement of both breasts and axillæ.

There was no complete cure in the 10 cases. The average age of the 3 who were considerably improved was 67·3 years. The treatment was of no value in 5 cases, whilst in 2 cases there was an adverse effect. In the case of carcinoma of male breast (aged 71) the effect of the stilbœstrol was to cause increased cellular activity of the breast cancer.

Professor B. W. Windeyer: My 10 cases were all cases of advanced carcinoma of the breast. 2 of them had had no previous therapy. The remainder had all had previous treatment, surgical removal in 5 cases and X-ray therapy to the primary lesion or to recurrences or metastases in 7 cases. Skeletal metastases were present in 3 cases. Pleural effusion was present in 2. They are, therefore, a series of very advanced cases.

The period of observation was on the average of five months' duration.

Of the 10 cases, 3 showed demonstrable improvement.

In none of the 10 cases has there been complete clinical disappearance of the growth, but 3 have improved.

In 4 cases no improvement has been noted and the disease has extended.

In the final 3 cases there has been no demonstrable clinical change since treatment was started. It is possible that there has been some retardation of the growth.

Stilbœstrol would appear to have had some effect in causing regression or retardation of growth. Its action, however, is uncertain and it has not caused complete disappearance of the disease in any case.

Professor E. C. Dodds: Stilbœstrol was produced as a substitute for œstrone and œstradiol and for experimental work of academic interest on the specificity of the œstrogenic reaction. It fulfilled all these expectations, and in addition it was found to control the symptoms of carcinoma of the prostate. If it has any action on cancer of the breast, this must be regarded as a kind of "pourboire". I am surprised that the doses given have not been much heavier in an attempt to evaluate whether the failure in a number of cases is due to a lack of sensitivity to the drug. It would also be interesting to try the other two synthetic œstrogens, namely hexœstrol and dienœstrol. The latter is a more powerful œstrogenic substance when administered by mouth. The definite improvement in a number of cases in women of menopausal and post-menopausal age requires very careful reviewing. The general systemic effect of œstrogens in the menopause is very striking and there is an immediate improvement in the woman's general condition and particularly a feeling of well-being. This must be allowed for. Finally, if the very excellent suggestion made by the Chairman is carried out—namely that the work should be continued—would it not be advisable to perform a rigid series of controls?

STILBŒSTROL CASES.

		Under 60			60 and upwards		
	No.	Improved	Not improved	Spectacular improvement	No.	Improved	Not improved	Spectacular improvement
Dr. S. Bryan Adams	4	1	3	—	6	3	3	1
Dr. R. McWhirter	20	3	17	—	17	3	14	1
Dr. J. Z. Walker	4	—	4	—	6	3	3*	
Dr. C. J. L. Thurgar	5	1	4	1	5	4	1	—
Dr. W. M. Levitt	10	—	10	—	1	1	—	—
Prof. B. W. Windeyer	8	3	5	—	2	—	2	—
Dr. F. Ellis	13	—	13	—	8	4	4*	2
Dr. Edith Paterson								
Stilbœstrol	8	—	8	—	5	2	3	—
Triphenylchloroethylene	13	5*	8	—	10	4	6	—
Mr. G. W. Blomfield	7	—	7	—	3	—	3	1
Dr. A. Haddow	8	1	7	—	5	3	2	—
	100	14	86	1	68	27	41	5

Under spectacular improvement are classified cases of which the following are typical : Ellis, Cases V. and VII. The breast tumour rapidly disappeared in both cases. The affected axillary glands also disappeared in Case V. In Case VII the axillary mass was reduced to one-fifth of its size.

* One male breast.

Section of Otology

President—T. B. Jobson, M.D.

[*March 3, 1944*]

Surgical Treatment of Otosclerosis

By I. Simson Hall, F.R.C.S.E.

That hearing can be improved by making an artificial opening into the labyrinth has been known since 1876, when Kessel first demonstrated the fact.

The main object of the surgeon since that time has been to replace the immobilized stapes by a movable membrane. Whether this is justified as the main aim is still open to proof, but the fact remains that mobilizing the fluid within the labyrinth results in an immediate and most dramatic improvement in hearing.

This may be accomplished in a variety of ways. It may be carried out with a small-sized mastoid gouge, used as a scraper, and a small hand lens, giving almost negligible magnification, or it may be carried out with elaborate equipment which is commonly used now. It is interesting to recall that one of my most successful fenestrations was done with the aid of the simpler equipment.

The technique for my earliest operations was very similar to that which I employ to-day, but without the specialized equipment. It is significant that improvement in results has kept pace with advance in technique.

Following Sourdille's advice I tried doing the operation in multiple stages, and experimented with cases using one to three stages. I came to the conclusion that there was no advantage in my hands of prolonging treatment, and I settled down to carry out the operation in one stage.

The position of the fenestra has also been the subject of some experiment. It has been placed in the canal itself following Holmgren's ideas. The same position was tried using Sourdille's technique. Then for a series of cases, a position over the ampulla was used. Again a reversion to the original technique was made, placing the fenestra over the ampulla, and that is the method used in the latest series.

A series of cases was also operated upon using the roof of the vestibule as advocated by Lempert, but, possibly by chance, this series was found to give inferior results, and the opening was taken more posteriorly to its former position. Perseverance with Lempert's position of the opening might have been found to give results similar to that obtained in the other methods, but the method used now is the easiest technique of all.

Approach to the middle ear is made through a post-aural incision or an end-aural incision. It does not matter which route is used provided that the operator is familiar with the method. I used the end-aural route in mastoid operations a sufficient number of times to make my operating time the same as when using the post-auricular route, which I take to mean that facility with either route was equal. Having reached this point, I decided that the post-auricular route was superior.

ANÆSTHESIA

The ideal anæsthetic for this operation is one which gives a slight degree of anæsthesia, lowers the blood-pressure, and is safe to use over a prolonged period. This anæsthetic has, unfortunately, not yet made its appearance. Local anæsthesia permits testing of the hearing on the operating table and gives a bloodless field. Pre-medication, with hyoscine and omnopon, is of great assistance, and I have tried avertin and other basal narcotics. A method I found very effective was to use local anæsthesia up to the opening of the labyrinth and when the patient became distressed, as is usual at this point, to give pentothal intravenously for as long as necessary.

At present a heavy pre-medication followed by light ether is the method used, and this is satisfactory on the whole as I have found that the delay caused by bleeding is more than compensated by the immobility of the patient and the greater speed which can be achieved under general anæsthesia. The small movements of the patient which occasionally take place under local anæsthesia are annoying when using the microscope, and general anæsthesia eliminates these.

THE OPERATION

The duration of the operation as a rule is about two hours, with about an hour and forty-five to fifty minutes' operating time.

The operation very closely follows the lines of the modified radical mastoid operation in the exposure of the labyrinth, with one or two slight modifications.

One of the most important parts of the first half of the operation is the formation of what is sometimes called the "meatal plastic". This is the mobilization of the postero-superior portion of the lining of the external auditory meatus and the membrana flaccida in a continuous flap, which is used to cover the new opening in the vestibule. This is a critical point of the one-stage operation as, should the flap be torn, the operation may have to be abandoned, or concluded as a two-stage operation.

Bleeding during the raising of the flap is apt to be troublesome but the preliminary infiltration of the area with normal saline and adrenaline solution helps considerably.

With the formation of the flap the usual plastic procedure for enlarging the external meatus is carried out according to the custom of the operator.

When the small flap is laid back the contents of the middle ear are open to inspection. The capsule enclosing the heads of the incus and malleus is incised with a fine-bladed knife; this frees the incus which can be removed without fear of damage to other structures.

The head of the malleus is then separated from the rest of the bone by division at the neck with a fine-pointed pair of scissors. This completes the first stage of the operation and the exposure of the horizontal canal and the roof of the vestibule.

For the second stage a microscope or other magnifying device is required, together with the drill, and the irrigating and suction apparatus.

The arranging of the apparatus makes a definite break in the operation, and advantage is taken of this by the surgeon and his assistant to change gown, gloves, &c. Fresh towels are spread and the trephining of the labyrinth is commenced.

Each operator will have his own preference for a particular type of drill, but many types are available, from the coarse cutting drill for the early stages, to the fine polishing stone for finishing the cavity. In the beginning any rough corners or pieces of bone are quickly smoothed off with a fast-cutting burr and the superficial layers of the vestibular roof are removed till the bluish cavity shows through.

When it is evident that the bony roof is becoming thin, the depression in the roof of the vestibule is carefully shaped and then polished. The edges of the bone covering the endosteum are then thinned with a fine burr till the endosteum is reached and the remaining bone and endosteum can frequently be removed with an elevator almost in one piece. The ampulla and canal can be identified immediately and the remaining shreds of endosteum and small pieces of bone are removed with scrapers, and other instruments specially made for the purpose. It is for this work that adequate magnification is absolutely essential. This completes the opening of the labyrinth. All that remains to be done is to spread the small flap over the fenestra and secure it in position with paraffin packs. The wound is closed completely.

POST-OPERATIVE TREATMENT

As a rule the wound is left undisturbed for one week when the pack is removed, the stitches are cut, and daily packing with paraffin gauze is resorted to. In the majority of cases a skin graft is inserted about the tenth day. A point which should be emphasized with regard to the after-treatment is that asepsis is essential. It is my experience that nothing leads so quickly to deterioration of hearing as infection of the cavity.

The duration of stay in hospital varies according to the patient's ability to attend for dressing. In the case of a patient living near, the stay in hospital is about two weeks.

Following operation there is evidence of labyrinthine disturbance, nystagmus to the opposite side, giddiness and past-pointing error. This lasts to a degree of discomfort for about four days after which it is noticeable to the patient only on movement. It may persist for three weeks or even longer and is noticeably slower to settle down in older people than in young.

The condition of the hearing immediately subsequent to operation is quite a good index to success, and I await with interest the report of the nursing staff. When they tell me that the patient is complaining about the noise in the ward on the morning after operation I anticipate a successful result although the hearing may shortly afterwards become poor, but when the patient shows apathy and lack of interest I suffer a corresponding disappointment. A small number of patients do not show the usual post-operative drop in hearing acuity and these, as a rule, are the most successful cases.

On the average about three to four weeks elapse before there is any noticeable improvement and the highest level is reached immediately after the ear cavity is healed, usually

in eight to ten weeks. This may amount to thirty decibels; but the average is about twenty-five decibels. Hearing tends to decrease after about two years till a permanent level of fifteen to twenty decibels gain is reached.

RESULTS OF OPERATION

In all, sixty-six operations have been carried out during the last six years. As technique has varied so greatly and so many methods have been tried it is impossible to assess the value of the operation by quoting tables of figures.

It is found in analysing results that improvement, if maintained for more than four months after operation, is likely to persist for some time, therefore cases operated upon within the last four months must be disregarded. Also, it is of no value to compare the earliest cases, operated upon with an equipment consisting of a hand lens and a scraper, with those operated upon with up-to-date methods, so that a number of the earliest cases must be excluded from analysis.

When this has been done we are left with a total of forty-five operations available for examination. Of these six have been lost sight of, and of the remaining number 20, or 51%, show improvement to-day.

These figures are of little practical value as they indicate the results of an operation which has differed from time to time in many particulars, and has been carried out on many types of case, suitable and unsuitable, and of varying ages.

One of the most frequent questions asked is whether the improvement which is gained will last. It is found that of cases operated upon prior to 1940, 36% have retained their improvement in hearing. In the period of twelve months, eighteen months ago to six months ago, the percentage improvement is 66%.

This affords a much fairer picture of the prospects of operation for, as might be expected, the most recently performed show the highest percentage of success. It is unlikely, however, that this comparative improvement is entirely due to the more recent date of the operations, for year by year the immediate failures are approximately equal, and the number showing late deterioration is fairly constant. The probability is that the latest group will show a higher percentage of final improvement.

In seeking an explanation of this several possibilities appear. The technique may have altered radically, the operator may have gained in skill, or the selection of patients may have been carried out in a more critical manner.

We may assume that technical efficiency has increased but this would account only for a very small part of the gain. Method, no doubt, is much more important and we find that removal of the incus gives an improvement rate of 54% as against 31% when it is retained. This may be interpreted in different ways. There is obviously no difference in the immediate results, and we must look for an explanation to some influence upon the remote effect.

I feel the most probable explanation of this is that the retention of the incus causes the fenestration to be carried out on the average more posteriorly on the canal, while removal facilitates the fenestration over the ampulla and the roof of the vestibule. A larger opening can be made there with much greater accuracy.

COMPLICATIONS

There has been one death in this series. This patient was a man aged 38, who died about six hours after operation, following an injection of a quarter of a grain of morphia which was given as routine to ensure rest after recovery from the anæsthetic.

Subsequent inquiry was strongly suggestive of an idiosyncrasy to morphia as he had nearly died some years previously, following an operation under local anæsthesia.

Apart from this case no patient has left hospital with other than a functioning labyrinth, showing that with proper precautions this operation can be undertaken without danger to life except such dangers as are inseparable from any major operation.

Cross-infections are not uncommon in a crowded nose, throat and ear department and as long as accommodation for segregation of these patients is not available, they will continue to give anxiety. Of such infections those leading to acute otitis media give the most anxiety and there have been three cases of this. Happily no serious harm resulted and the patients recovered without further trouble. In one case a particularly good result was obtained, in the others, the hearing was the same as before operation.

Cavity infections are a particularly unfortunate complication and unless checked at once are almost certain to ruin any chance of improvement in hearing. There have been no cases of facial paralysis, and no cases of labyrinthitis.

OTHER EFFECTS OF OPERATION

Confusion of sounds is the rule after operation, and it is not easy for a patient at first to pick out the voices from the mass of amplified noise which surrounds him, and I

perilymph and endolymph spaces through a dry radical mastoid cavity for intractable vertigo, recovery has been uneventful.

So far, I have only made use of the closed method of access and in the first four cases of otosclerosis on which I operated, this stage was carried out under general anæsthesia, the opening of the perilymph space being carried out under local anæsthesia after an interval of one or more weeks. The meatal approach as advocated by Lempert offers certain advantages which, in accustomed hands, probably outweigh the difficulties of working in a restricted field.

Whatever method of approach is used it is, of course, essential to achieve complete hæmostasis before the second stage is embarked upon. It was because of the difficulty of checking oozing that I abandoned the two-stage operation, though it is possible that there would have been less trouble in this direction had I allowed a greater interval to elapse between the two stages.

(2) *Opening the perilymph space.*—This stage is also part of the operation that Hallpike and I described at this Section last year for the relief of Ménière's disease (*Proceedings*, 1943, 36, 543).

In the first place this stage demands a certain degree of magnification if it is to be carried out accurately, safely and with ease.

Once one has become accustomed to it, the advantages of working in a magnified field, such as is provided by a binocular dissecting microscope giving ten diameters of magnification, are sufficient to warrant urging its use for this stage of the operation.

I have found that a portable dental machine driving a diamond paste burr at 3,000 r.p.m. a convenient and very safe way of making the window in the bony external canal. It is advisable to make the opening in the anterior and inferior aspect of the convexity of the bony canal because in this way there is less chance of damaging the membranous canal which is usually in contact with the inner wall of the bony canal in the upper part of the convexity. At this stage I usually remove the incus which otherwise is liable to be damaged by the drill and this allows a much greater freedom of manœuvre.

The dry, powdery bone dust that is thrown off by the drill can at this stage be easily removed by following the drill in its excursion with a fine suction tip. This enables the fundus of the trough so formed to be clearly seen the whole time, and the dark line marking the approach to the perilymph space may be recognized in good time. This is the time to make sure that all the bone dust is removed for once the perilymph oozes out, it is not at all easy to remove all traces of sodden bone dust.

As the innermost layer of bone is gently thinned down, perilymph slowly oozes through one or more very tiny holes, although the main mass of bone is apparently intact. In the conscious patient I have noticed that at this stage vertigo is complained of and may be sufficient to cause some distress. There is not, however, any noticeable improvement in the hearing. Very soon the thin irregular lamina of bone breaks away and it is at this moment that a dramatic improvement in the hearing takes place. This thin flake of bone, that may be likened to a flake of what we call a "cream cracker biscuit", often breaks into several pieces, the removal of which by means of fine dental probes may be troublesome and tedious. Any attempt to remove excess perilymph by suction, or worse still by cotton mops, is very liable to drain it away, leaving the perilymph space of the canal temporarily dry. This will, of course, increase the difficulty of removing any retained bone dust or chips.

Also, the displacement and apparent collapse of the membranous canal cannot, I feel, be a good thing. I have not been able to record any constant variation between the amount of perilymph exuded in cases of Ménière's disease or otosclerosis or indeed in the amount seen in any two cases of the same disease. If by chance it has been drained away, it usually seems to re-form within a few minutes and it seems to re-form more quickly if there is any venous obstruction. Once the initial outflow has taken place it does not, as a rule, flow over again, at any rate within the half-hour or so that I have watched these cases. Nor have I ever seen anything to suggest any escape of perilymph after the operation. This is, I think, because a film of fibrin seals over the opening fairly quickly.

With regard to the possible danger of blood entering the perilymph space and jeopardizing the result, I do not think that this can happen easily if there is a good head of pressure of perilymph, though I do not think because of this precautions against bleeding should in any way be relaxed.

The membranous canal is surprisingly tough and will stand quite a lot of handling without breaking. This is a source of great comfort, though I would not like to say what indirect effects might follow unnecessary trauma and I feel sure that in operations for otosclerosis the membranous tube should, if possible, not even be touched.

(3) *The protection and maintenance of the opening.*—So far this has proved to be the most difficult obstacle to overcome and I fear that I have no useful contribution to offer to the discussion. Lempert, Canfield, Campbell and Shambaugh, to mention a few, have made special studies of the factors that influence the closure of the window by new bone or fibrous tissue formation, and it is considered that such closure is responsible for the failure to maintain the initial improvement in hearing. So far I have only used the closed method employing flaps of mucoperiosteum and fibrin to cover the window, but it would seem that the best results follow an open operation where flaps of tympanic membrane are laid against the window. The transient reaction that follows does not appear to have an unfavourable influence on the final result. I notice that Campbell advocates thinning down of the bony canal without actually opening the perilymph space and it would be very interesting to hear from other speakers if they have any experience of this procedure.

Results.—My results so far have been uniformly disappointing. In the eight cases upon which I have operated all experienced an immediate, and in some instances remarkable, improvement in hearing but without exception the hearing gradually deteriorated to the pre-operative level within a month. In no case has it become appreciably worse within the period that they have been under observation. In every case the post-operative vertigo and nausea, though of short duration, have been more severe than after labyrinthectomy for Ménière's disease. This is not surprising, as presumably the otosclerotic

have found that some did. not try and so failed to make use of an obvious increase in acuity.

An interesting phenomenon has been observed in connexion with this confusion which is based on the failure to orientate sounds. This is illustrated by the statement of a patient that she frequently found that she looked to her left when someone spoke on her right. The same condition was evident in a patient who said she felt that the tram-way-cars were chasing her on to the pavement; apparently she saw the car approach-ing but the sound seemed to be behind her on the pavement. This is probably explainable on a purely physical basis, but it opens up some interesting questions for investigation.

Another circumstance which is of interest is the influence of pregnancy upon the regained hearing. Two patients have become pregnant subsequent to operation. In one case hearing deteriorated to some extent, in the other hearing remained stationary.

The question may be asked whether the operation, when successful, unfits the patients in other ways for employment. In the majority of instances the patients are sedentary or office workers, and physical effort plays a small part in the earning of a livelihood. There have been instances where the operation has had some effect on capacity for work. This was illustrated recently by the experience of one young man, a riveter by trade, who had a slight sensation of giddiness on stooping suddenly, and when riveting inside a ship's boiler he found the reverberation too much for him and had to be shifted to an outside job. This disability, however, did not lessen his usefulness as a worker.

SELECTION OF PATIENTS

Selection of cases has a great deal to do with results. In the earlier series almost any type of patient suffering from middle-ear deafness was accepted provided they showed no signs of middle-ear disease—cases of mixed middle- and inner-ear deafness were pur-posely selected to ascertain whether the improvement of the middle-ear component of the deafness would result in useful hearing. We know from that experience that such patients derive no permanent benefit and so they are now refused. Sinusitis and naso-pharyngeal infections are contra-indications to operation.

There are certain common characteristics in those showing improvement. The majority are young—usually under thirty years—the deafness is not extreme, there is neither sign nor history of middle-ear disease, and there is no nerve deafness. A family history of deafness is regarded as confirming the diagnosis and favouring a successful result, and finally the patient must be intelligent. This is necessary so that the patient may re-educate himself to use the regained hearing.

Many patients have been under observation for a period of years. Repeated audiometer records are made, and operation is undertaken only when there is strong evidence of steady deterioration of hearing.

Routine tuning fork tests are done but the audiometer record is the chief guide though, of itself, it is not always reliable in nerve deafness. Not having two similar audiometers for tests, I rely for confirmation on the monochord. Lack of appreciation of the upper tones by bone conduction has proved a contra-indication to operation, and where this is discovered, I always now refuse the patient for operation.

Some failures may be attributed to age; also infection of the cavity either during the convalescent period or later, owing to accumulation of wax or other causes, always means loss of hearing. Technical failure plays its part though I have notes of only one case where a complete breakdown in the electrical system contributed to failure. In another case obvious signs of previous labyrinthitis were found at operation.

CLOSURE OF FENESTRA

It seems that patency of the fenestra is of the utmost importance in retention of im-provement in hearing. In many of these cases listed as failures, a fistula sign can be elicited but one can readily recognize the loss of sensitivity which presages failure.

There is a tendency in some cases for the hearing to remain stationary while that of the other ear continues to deteriorate. This can be shown clearly by audiogram.

It seems that now we have reached the stage when technical advancement has almost ceased and the future of this operation rests upon the results of research into the question of bone regeneration.

(The paper was illustrated with lantern slides showing the various stages of the operation, apparatus, and audiometer records of various types of cases.)

Mr. Terence Cawthorne: I am most interested in the technique of and the effects produced by opening the perilymph space of the external semicircular canal and it is about this particular procedure that I should like to give you my experiences.

It will be convenient to consider the surgical treatment of otosclerosis in three stages:

(1) The surgery of access.—It has been clearly shown by Sourdille, Lempert and others that the open operation offers a greater prospect of success than the closed, without any undue risk of infection spreading inwards. In the four cases in which I have opened the

carried out under local anæsthesia and all got the immediate dramatic improvement in hearing, but of the seven cases within six weeks five had gone back to the pre-operative degree of hearing. Unfortunately the war had prevented a proper follow-up but he saw one case last year quite by accident, when the lady was sent to him by a gynæcologist to ask if it was safe for her to have a baby, and he found the hearing had remained with a considerable degree of improvement over the five-year period.

Mr. C. A. Hutchinson said that a point apt to be overlooked was that in otosclerosis one was dealing with a general systemic disease and not merely with a local condition. Certainly the most interesting and probably the most correct of the many theories as to its ætiology was that put forward by Eckhert Moebius; accordingly surgery combined with appropriate general treatment offered a better chance of success than pure surgery alone. In May 1939 he had shown one case in the Section which after the lapse of nearly five years still retained a very considerable portion of the primary improvement secured.

He was particularly interested in the fact that the many and varied initial techniques had become more or less standardized; all workers stressed the importance of the removal of bone chips, all used practically identical instruments, and all opened the labyrinth in almost identically the same position.

Like Mr. Simson Hall, he employed a continuous but controllable saline stream to remove bone chips, but added a few drops of adrenaline to help control hæmorrhage.

With regard to anæsthesia he had found gas-oxygen-trilene combined with omnopon-scopolamine premedication produced least hæmorrhage during and after operation.

He envied Mr. Simson Hall his operating microscope. Unfortunately his own work had been interfered with by three years' war service; he had tried on his return to obtain a similar instrument, but had failed and was therefore grateful to Major Fowler for his suggestion of an alternative such as mineralogist's binoculars. He had been using a Harman loupe, but its grave disadvantage was its short focal length causing insufficient room for instrumentation and difficulty in securing adequate illumination of the field of operation.

Mr. Simson Hall (in reply) said that in his opinion irrigation under complete control, and either constant or intermittent as required, formed the solution to many difficulties such as bleeding and troublesome bone dust. Adequate magnification was also of very great importance, in his opinion about 10 diameters was the optimum. This could be increased, however, in special circumstances, e.g. by "eyepiecing". The working distance was of importance and his instrument allowed about 15 cm. but what was of equal importance was the access which the instrument provided. Some dissecting microscopes were very bulky.

Selection of patients was still one of the most difficult points. He agreed that extreme deafness was a contra-indication to operation. An attempt had been made to investigate patients as completely as possible, particularly in conjunction with an endocrinologist. Results so far were inconclusive.

Deterioration of hearing following operation had to be judged not only by the decibel loss from the original post-operative gain, but in relation to the probable position of the hearing had no operation been performed. That is to say, although the average immediate gain of 25-30 decibels was found as a rule to have sunk to a permanent level of 10-15 decibels after two or more years, the real gain to the patient was this 10-15 decibels plus the amount of deterioration in the opposite ear. That figure represented the real gain to the patient from the operation.

The patients experienced a sense of relief and new hope in their lives which was reflected in their appearance and outlook.

[May 5, 1944]

DISCUSSION ON THE USE AND MISUSE OF SULPHONAMIDES IN OTITIS MEDIA

Mr. W. Stirk Adams: Since 1936 M & B 693 has been part of the standard treatment of all cases of acute otitis media admitted to my care in the hospital, and though the other members of the group, M & B 760, sulphamethazine and sulphadiazine have been tried, we find the most consistent results have been attained with M & B 693, though occasionally we have switched to M & B 760 with satisfactory results in a case which was responding badly to M & B 693.

I do not regard the use of sulphonamides as replacing other treatment, but regard it as of prime importance in stemming the invasion by the infection, while the local and general immune bodies are being developed in quantities required for its elimination.

The results obtained in cases of acute otitis media in the Children's Hospital, Birmingham, in the last pre-sulphonamide year, 1935, compared with those obtained in 1942, show that out of 250 admissions 63% required a cortical mastoid operation in 1935, while in 1942, out of 350 admissions only 32% required this operation.

has an active labyrinth, whilst the vestibular function in those cases of Ménière's disease submitted to operation is always diminished.

This post-operative reaction cannot be explained entirely on the grounds of a serous reaction because it appears as soon as the perilymph space is opened and is at its worst directly after the operation.

There are several aspects of the fenestration operation for otosclerosis that require further investigation and perhaps the most important is why does the hearing improve when the perilymph space is opened? Is it because sound waves are transmitted through the opening to the basilar membrane and if this is so, by what route do they travel? And why do we not hear of more cases in which loud sounds cause vertigo?

There was one case of Ménière's disease in which the perilymph space was opened without interfering with the membranous canal. Subsequently it was found that the patient gave a very noticeable vestibular reaction to loud sounds. This was so troublesome that within a month it was necessary to remove the membranous canal.

Major E. P. Fowler, Jr., U.S.A.M.C.: Perhaps if the causes of bony closure in monkeys were examined, they would help in humans. The most potent cause of closure is undoubtedly bone dust and bone chips. Infection in the flap or in the labyrinth also produces closure. There was some question whether premedication with sulphonamides or penicillin might not help in this connexion. The position of the fistula theoretically also would affect closure. If the fistula were made where there was much endochondral bone and little periosteal bone the fistula would not close, for endochondral bone does not grow as does periosteal bone. The periosteal bone should be removed carefully for it is potentially a rapid bone former. Epithelium apparently inhibited bone growth in some monkeys. The fistula should be made with a burr and the edges highly polished. Colonel Canfield has done experiments showing the bone growth is inhibited by the use of a polishing burr.

As to the position of the fistula on the semicircular canal itself, Major Fowler said the thinnest bone was over the white bright smooth area which is often considered to be the ampulla. Actually the membranous ampulla was much further forward than one would think. It is over this that Lempert makes his fenestra nov-ovalis. Lempert had described something called the "dome" of the vestibule which is an unfortunate term. If one really went through the top of the vestibule, one would have to cut through a great deal of bone and through the nerves of the labyrinth, which was technically difficult in the living subject.

There was one other thing which might cause closure of fistula. One of his early cases had a very severe otosclerosis, and when she was reopened it was found that the first fistula had closed, and there was a most extraordinary coloured bone over the whole canal; it looked yellow instead of the usual ivory colour. The endochondral capsule was invaded by otosclerosis to the area ordinarily used for these fistulas. When extensive otosclerosis is suspected the operation should not be performed in old people nor in very deaf people.

With regard to dizziness from loud sounds he thought the American underground railway was louder than the British for all his patients had complained of dizziness when travelling on the underground railway.

He had experimented with microscopes for a long time and finally found that a pair of binoculars such as used by mineralogists proved most useful. It gave him 26 cm. to work in and to shine the light through and could be easily surrounded by a sterile shield. He used 7 to 10 magnifications.

Surgeon-Commander E. R. Garnett Passe (*in absentia*): One of the most important problems still to be solved in otosclerosis is that of diagnosis; and to add further to the confusion we now have blast deafness, of which I have seen many cases of late. The audiometer chart alone does not differ in many ways from that of the early perceptive deafness and we will have to be on the lookout for these cases before making a diagnosis of otosclerosis. The history alone of blast or gunfire injury is not in itself sufficient. In September 1939 (*J. Laryng. Otol.*, 54, 566), I recorded the results of surgical treatment of 14 cases of otosclerosis performed during the preceding eighteen months, using both Holmgren's and Lempert's techniques. However, only one of these cases now shows any improvement. Since then I have used Lempert's vestibular dome as the site of fenestration and I am hopeful that the immediate good results will prove more lasting. To my mind it does not matter where the site of fenestration is so long as the perilymph is decompressed and the opening made permanent, or at least permanently membranous. Contrary to Nasiell's article I am further able to support Meyer's work on decompression of the C.S.F., for during the last two years I have had temporary improvement in hearing on removal of large quantities of C.S.F. and replacement by air, with the effect that several officers and men in the Royal Navy have been able to continue with their work and they willingly submit to the decompression from time to time.

To my mind the essential underlying cause of otosclerosis is a vasomotor disturbance, as described by Wittmaack. According to the theory of Leriche and Policard, in order for calcification to occur there must be present three factors—an ossifiable medium, a rich source of calcium locally and a poor blood supply. The blood supply to the bony parts chiefly affected in otosclerosis is derived from branches from both the internal auditory and the internal carotid arteries. The neurovascular supply of these arteries is via the plexus surrounding the vertebral and internal carotid arteries and there is some belief that the vasoconstrictor fibres are passed by the 1st and 2nd divisions of the 5th cranial nerve. This opens up further possibilities in the surgical treatment of otosclerosis for it is possible that there may exist an anatomical abnormality in the course of this nerve supply which interferes with its normal function, and I think the future treatment of otosclerosis lies not in the organ itself but at some faulty part of its peripheral control.

Mr. Walter Howarth said that he was very interested in the end-results of these cases because he thought that as the years passed they were apt to deteriorate. His experience of this operation of labyrinthine fenestration amounted to seven cases which he did in 1937 following out Holmgren's technique, but the results were very disappointing. They were

carried out under local anæsthesia and all got the immediate dramatic improvement in hearing, but of the seven cases within six weeks five had gone back to the pre-operative degree of hearing. Unfortunately the war had prevented a proper follow-up but he saw one case last year quite by accident, when the lady was sent to him by a gynæcologist to ask if it was safe for her to have a baby, and he found the hearing had remained with a considerable degree of improvement over the five-year period.

Mr. C. A. Hutchinson said that a point apt to be overlooked was that in otosclerosis one was dealing with a general systemic disease and not merely with a local condition. Certainly the most interesting and probably the most correct of the many theories as to its ætiology was that put forward by Eckhert Moebius; accordingly surgery combined with appropriate general treatment offered a better chance of success than pure surgery alone.

In May 1939 he had shown one case in the Section which after the lapse of nearly five years still retained a very considerable portion of the primary improvement secured.

He was particularly interested in the fact that the many and varied initial techniques had become more or less standardized; all workers stressed the importance of the removal of bone chips, all used practically identical instruments, and all opened the labyrinth in almost identically the same position.

Like Mr. Simson Hall, he employed a continuous but controllable saline stream to remove bone chips, but added a few drops of adrenaline to help control hæmorrhage.

With regard to anæsthesia he had found gas-oxygen-trilene combined with omnopon-scopolamine premedication produced least hæmorrhage during and after operation.

He envied Mr. Simson Hall his operating microscope. Unfortunately his own work had been interfered with by three years' war service; he had tried on his return to obtain a similar instrument, but had failed and was therefore grateful to Major Fowler for his suggestion of an alternative such as mineralogist's binoculars. He had been using a Harman loupe, but its grave disadvantage was its short focal length causing insufficient room for instrumentation and difficulty in securing adequate illumination of the field of operation.

Mr. Simson Hall (in reply) said that in his opinion irrigation under complete control, and either constant or intermittent as required, formed the solution to many difficulties such as bleeding and troublesome bone dust. Adequate magnification was also of very great importance, in his opinion about 10 diameters was the optimum. This could be increased, however, in special circumstances, e.g. by "eyepiecing". The working distance was of importance and his instrument allowed about 15 cm. but what was of equal importance was the access which the instrument provided. Some dissecting microscopes were very bulky.

Selection of patients was still one of the most difficult points. He agreed that extreme deafness was a contra-indication to operation. An attempt had been made to investigate patients as completely as possible, particularly in conjunction with an endocrinologist. Results so far were inconclusive.

Deterioration of hearing following operation had to be judged not only by the decibel loss from the original post-operative gain, but in relation to the probable position of the hearing had no operation been performed. That is to say, although the average immediate gain of 25-30 decibels was found as a rule to have sunk to a permanent level of 10-15 decibels after two or more years, the real gain to the patient was this 10-15 decibels plus the amount of deterioration in the opposite ear. That figure represented the real gain to the patient from the operation.

The patients experienced a sense of relief and new hope in their lives which was reflected in their appearance and outlook.

[May 5, 1944]

DISCUSSION ON THE USE AND MISUSE OF SULPHONAMIDES IN OTITIS MEDIA

Mr. W. Stirk Adams: Since 1936 M & B 693 has been part of the standard treatment of all cases of acute otitis media admitted to my care in the hospital, and though the other members of the group, M & B 760, sulphamethazine and sulphadiazine have been tried, we find the most consistent results have been attained with M & B 693, though occasionally we have switched to M & B 760 with satisfactory results in a case which was responding badly to M & B 693.

I do not regard the use of sulphonamides as replacing other treatment, but regard it as of prime importance in stemming the invasion by the infection, while the local and general immune bodies are being developed in quantities required for its elimination.

The results obtained in cases of acute otitis media in the Children's Hospital, Birmingham, in the last pre-sulphonamide year, 1935, compared with those obtained in 1942, show that out of 250 admissions 63% required a cortical mastoid operation in 1935, while in 1942, out of 350 admissions only 32% required this operation.

TABLE I.—OTITIS MEDIA 1942.

(1) *Duration of Aural Symptoms Prior to Admission.*

Days	1	1–5	5–7	7–10	10–14	14–21	21–28	28–35	35–42	42–49	49–56	Months 2–4	4–6	6–8	8–12	Over	Not known
Number of cases	9	61	49	25	47	34	27	6	13	3	12	21	7	4	11	20	1

(2) *Duration of Aural Discharge Prior to Admission.*

Days	1	1–5	5–7	7–10	10–14	14–21	21–28	28–35	35–42	42–49	49–56	Months 2–4	4–6	6–8	8–12	Over	Nil
Number of cases	15	64	38	18	35	25	19	3	2	3	5	11	3	4	5	9	91

(3) *Duration of Hospital Stay.*

Days	1–5	5–7	7–10	10–14	14–21	21–28	28–35	35–42	42–49	49–56	Months 2–4	4–6
Number of cases	15	7	25	26	37	42	24	31	12	15	18	9

(4) *Age-group.*

	Under 1	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12	12–13
	68	45	42	27	30	40	31	18	12	12	11	8	6
Previous otitis	14	17	7	6	5	7	5	3	5	3	2	3	

This is an analysis of the cases admitted with acute otitis media in 1942. From the first and second sections recording the duration of aural symptoms before admission it is clear that the majority of cases are received at too late a stage of the invasion for successful sulphonamide treatment, though most of them had already received out-patient treatment. The third section records the duration of hospital stay required for resolution. The analysis has not been carried far enough to show that the longest in-patient treatment is required in the youngest children.

The fourth section is an analysis by age-groups, and reveals the frequency of previous attacks of acute otitis media.

TABLE II.

Number	Dry on M & B 693	Dry on M & B 693 and incision	Cortical mastoid	Transfer	Died		
Under 1 year	21	16	12	15	4		
1–2	13	10	10	12			
2–3	7	15	9	11			
3–4	8	8	4	6	1		
4–5	7	6	4	13			
5–6	13	9	8	9		Silver nit.	1
6–7	6	12	4	8		Furuncle	1
7–8	5	6	3	4			
8–9	5	1	3	2		Tonsillectomy	1
9–10	4	2	4	2			
10–11	1	2	3	5			
11–12	3	2	—	1		Ultraviolet light	1
12–13	1	2	2	1		Granuloma	1
Total	94	91	66	89	5		5
Transfers	22	19	42			Diagnosis not confirmed	
Total of cases	116	110	108	Without treatment 6		5	

32·1% cortical mastoids.

An analysis of the results of treatment by age-groups. The cases transferred were sent to other hospitals outside the service of the Children's Hospital (Fever Hospitals and E.M.S. Hospitals) before the conclusion of treatment for the condition. It will be noted that two-thirds of the cortical mastoids opened were so transferred. This was done because of the pressure on in-patient accommodation in the Children's Hospital.

Of the cases transferred and recorded as dry on sulphonamide, and on sulphonamide and incision of the drumhead, no follow-up has been possible, and it may prove that a few of these required a cortical mastoid operation. The number is, however, small in relation to the full figures, and is unlikely to upset the validity of the conclusions arrived at.

There was no change in the type of case admitted during these two years, nor of the severity of the prevailing infection.

Method of Selection of Cases for Admission

The cases may be admitted either from the casualty department or on receipt of a telephone request from the patient's medical adviser; but chiefly from the out-patient department. They comprise the more serious types of infection which have proved resistant to treatment, or which may respond badly to ambulant treatment. In this out-patient department some 500 new cases were received in 1935. During successive years the number has steadily risen until now we have 1,200 new cases under treatment each year.

The 350 cases admitted in 1942 can be divided into: (1) Primary otitis media, 264 cases, 75% of the series with an operative mastoid rate of 28%. This group comprises all cases where there is no history of previous otitis media. (2) Relapsing primary otitis, 39 cases, 11% of the series. This is a subdivision of the first, and shows cases where a dry ear was obtained on an initial course of sulphonamide treatment but relapsed on withdrawal of the drug; a second course of sulphonamide was then given, in some cases with a satisfactory result. (3) Recurrent otitis media, 86 cases, 25% of the series with an operative mastoid rate of 38%.

Here the operative rate is higher than in a primary otitis, and this is borne out by our experience that it is more difficult to obtain resolution of the infection by sulphonamide treatment in a mastoid previously involved than in a virgin mastoid.

Although these figures show that 25% of all admissions had had a previous otitis media, we should not regard this as the true incidence of recurrence; recurrent otitis media is recognized as a more resistant infection to treatment, and cases would normally be admitted to the ward. The true incidence of recurrence is probably in the region of 10% and may be less.

Management of Cases

(a) Adequate nursing care is essential for at least a week after all signs and symptoms have disappeared. They are retained in hospital for a week after the end of the sulphonamide course, as it is found that relapse is most likely to occur on the fourth day after the course of sulphonamide has ended.

(b) Drumhead incision where evidence of tension is present, or in the cases where spontaneous perforation has occurred without elimination of pain or pyrexia.

(c) *Sulphonamide dosage.*—Although estimation of the blood level of sulphonamide is advisable, an empirical dosage must be employed. It is essential to use a heavy loading dose during the first twenty-four-hour period, and in practice it is found that in children between 3 and 6 years old an initial dose of 2 g. followed by 1 g. four-hourly in the first day, dropping to 4 g. on the second day, and 3 g. in each succeeding day for the next four days gives the best results.

The change in the dose is most easily made in the 2 a.m. feed. In infants a dose of 1 g. per day for every 7 lb. weight is a satisfactory working rule with sulphadiazine.

My House Surgeon, Mr. A. F. Alvarez, has carried through a valuable investigation on the relation between the quantity of the drug given, the urinary output and the blood level of sulphonamide obtained in a series of 13 cases. They fall into three groups.

In the fitter children the blood level quickly reaches its peak whilst in those children who appear more ill, and less robust, the blood level rises gently. He also finds the urinary output of sulphonamide per day varies considerably from case to case, and cannot be relied on for information of the sulphonamide blood level maintained in the patient.

In the clinical management of these cases a progress chart showing the amount of discharge from the external canal and (if opened) the mastoid wound is invaluable in assessing progress. On these charts the Charge Nurse records her estimate of the amount of discharge from each ear daily under one of four headings, Excess, Medium, Small or Dry.

One case illustrates a sulphonamide failure in a long-standing infection. Child aged 7 years, admitted with a history of apparent acute otitis on the right side. Treatment by right drumhead incision and a course of 20 g. sulphonamide failed to promote resolution and twelve days later he developed a pyrexia of 103°. A cortical mastoid operation was performed. Later we learned that he had had scarlet fever five months before, and had been sixteen weeks an in-patient at the City Fever Hospital. Towards the end of that illness his right ear had discharged for twelve days, six weeks before we received him, and at the Fever Hospital he had already had two courses of sulphonamide.

Another case which illustrates the failure of sulphonamide, and the severity of the toxic reactions that may occur in infantile infections, occurred in an infant of six months. He was admitted with a history of three weeks' earache, drumhead incision prior to admission, and continuing aural discharge and earache. He had a 10 g. course of sulphonamide; although the discharge cleared, a fortnight after admission a raised temperature, rising pulse-rate and frequent stools suggested a continuing aural infection. Both drumheads were again incised and five days later a bilateral cortical mastoid operation was performed as his condition was rapidly deteriorating.

From this time on his condition slowly improved, as usual the weight being the last to recover. A journey of 40 miles by ambulance to a country hospital, and a change of nursing staff, produced a minor relapse from which, however, he soon recovered.

Conclusions

(1) Always use sulphonamide in the early phase of invasion.

(2) Even when coming late under treatment up to the third week of infection there is no objection to the use of sulphonamide if no surgical contra-indications are present.

(3) The contra-indications are, with free discharge from the middle ear: (a) toxic appearance; (b) continued pyrexia; (c) severe deafness—below 18 in. for whispered voice; (d) any evidence of intracranial spread. All these are indications for exploration of the mastoid—which may of course be followed by sulphonamide therapy.

(4) At whatever stage of an otitis, incision of the drumhead is essential where evidence of tension is present before sulphonamide results can be obtained.

Misuse.—(a) By failure to appreciate the objective; (b) by inadequate dosage; (c) by mistiming the application of sulphonamide; (d) by continuing the application once evidence is present that the infection is not responding; (e) by continuing the use of the drug for more than ten days or exceeding 30 g. in a course; (f) by asking the drug to

produce results under unfavourable local or general conditions. *Local*: Infection with fluid under tension; *General*: Ambulatory treatment; and where frequent recurrences of infection have occurred in the same mastoid.

In using sulphonamides in adults my best results were obtained by combination of sulphonamide early and superficial X-rays later.

Sulphonamide in chronic otitis is best used as a powder locally of 25% strength in boric acid powder.

Mr. G. Ewart Martin: Our departmental records indicate that ear cases are coming later to hospital for specialist advice. In many instances pain had been present for some days but having been given tablets by the doctor, the temperature and general well-being appeared normal; advice was only sought because of the deafness, yet there was pus behind the drum.

With what must be termed indiscriminate use of sulphonamides deafness is a much more common result of an acute ear than it was in the past.

Sulphonamides are not to be disparaged in the treatment of otitis media—far from it, as they have made the otologist's work very much easier. But the benefits are being negatived by faulty prescribing.

Here is a brief résumé of the cases of acute otitis media, in my own department, for the five years previous to the use of sulphonamide and the five years after its use. From our records sulphonamide, in the form of prontosil, was used in my department in 1937.

CASES OF ACUTE SUPPURATIVE OTITIS MEDIA SEEN IN THE OUT-PATIENT DEPARTMENT OF THE ROYAL INFIRMARY, EDINBURGH, WITH EITHER A RECENTLY RUPTURED DRUM OR REQUIRING PARACENTESIS.

		Acute otitis media (suppurative)	Mastoid complications following on the acute ear	Intracranial complications	Deaths
1932	...	198	69	5	1
1933	...	243	94	10	4
1934	...	244	73	11	3
1935	...	243	56	9	2
1936	...	266	62	4	1
1937	...	222	40	2	1
1938	...	224	33	6	2
1939	...	226	31	1	1
1940	...	203	32	2	—
1941	...	168	13	2	2
1942	...	178	26	2	1
1943	...	169	23	3	1

It has not been possible to include patients who went to an outside hospital instead of the Royal Infirmary, Edinburgh, in 1941 to 1943 which will account for the apparent drop in the number of cases of acute otitis media (suppurative).

It will be seen that in 1932 35% of acute suppurative otitis media developed mastoid complications, in 1933 38%, while in 1941 9% and in 1942 20% required mastoid interference. The percentage of intracranial complications remains about the same, if anything, a little higher, or so it would appear in comparing the 10% of 1933 with the 15% of 1941. The death-rate of intracranial complications is about the same, but the use of sulphonamide has revolutionized the treatment of meningeal complications.

Last year of the 23 cases developing mastoid complications of an acute suppurative or perforative otitis media 3 developed meningitis, and it is interesting to give a synopsis of these 3 cases.

(1) Female, aged 6. Admitted to hospital on 3.8.43 with a history of having had an acute otitis media on 14.7.43 when the drum had been paracentesed. She had been given fairly large doses of sulphonamide.

On admission there was the suspicion of a Kernig's sign. Lumbar puncture was clear. A Schwartze operation was done the following day. The temperature remained high and a lumbar puncture showed cloudy fluid with a cell count of 5,000 and Gram-negative bacilli present on culture. She was kept on sulphonamides and altogether had 198½ g. of the sulpha preparations.

4.8.43: Sulphanilamide L.S.F. intramuscularly	30 c.c. =	4½ g.
5.8.43 to 9.8.43: M & B 693 intramuscularly		17 g.
5.8.43 to 9.8.43: M & B 125 tablets		14 g.
13.8.43 to 20.8.43: M & B 693 intramuscularly		23 g.
13.8.43 to 20.8.43: M & B 125 tablets		23 g.
20.8.43 to 3.9.43: sulphadiazine tablets		71½ g.
3.9.43 to 11.9.43: sulphaguanidine tablets		45½ g.
Total sulphonamides 198½ g.		

Patient was also given pentnucleotide injections intramuscularly, 56 c.c. Recovery was complete. Patient was in hospital for seven weeks and when seen one month ago the ear was dry and healthy. The only difficulty was that she had a slight drop foot on the right side, possibly secondary to the intramuscular injections.

(2) Female, aged 33. Admitted on 28.12.42 with a definite mastoid infection following an acute otitis media which she developed ten days previously. She had had sulphonamide—about 2 tablets of M & B 693 each day before admission. There was no description of the ear.

On admission there was a posterior perforation. Swelling over the mastoid, slight neck retraction and a Kernig's sign was present. C.S.F. was turbid with a cell count of 2,000. The right mastoid was opened. There was a large pool of "laked" pus in the mastoid which was drained.

Patient was put on large doses of sulphonamide.

28.12.42 to 31.12.42:	M & B 125 tablets	..	..	..	16 g.
28.12.42 to 8. 1.43:	M & B 693 intramuscularly	..	..	..	31 g.
8. 1.43 to 11. 1.43:	M & B 125 tablets	..	..	..	13 g.
11. 1.43 to 12. 1.43:	Sulphadiazine tablets	..	..	..	7 g.
12. 1.43 to 16. 1.43:	M & B 693 intramuscularly	..	..	..	23 g.
12. 1.43 to 14. 1.43:	M & B 125 tablets	..	..	..	10 g.
14. 1.43 to 19. 1.43:	135 hypiloid sulphonamide	..	..	..	31 g.
19. 1.43 to 23. 1.43:	M & B 125 tablets	..	..	..	12½ g.
	Total sulphonamides = 143½ g.				

There was a growth of hæmolytic streptococci from the mastoid and Gram-negative bacilli reported from the C.S.F. These were seen in further specimens, with a great number of pus cells.

Recovery was complete with a healthy ear and a hearing of a whisper at 8 ft. The patient has been back at work since the middle of May 1943.

(3) *Male, aged 12. Admitted on 22.11.43 with a history of pain in the ear for three days.* On admission patient was restless. There was neck rigidity and Kernig's sign.

The right drum was incised and the organisms showed a pneumococcus. Lumbar puncture showed a cell count of 15,000 and a type 8 pneumococcus.

The patient was given sulphanilamide intramuscularly and sulphapyridine by the mouth every four hours for five days. The temperature came down in three days to normal but there was a relapse. He was transferred to the neurological department and there the sulphonamide was continued by drip along with anti-pneumococcal serum. He showed little response and died on 9.12.43.

The percentage of complications in otitis media, first mastoid, second intracranial, and third general, is still too high. Deafness as an after-complication is on the upgrade.

I am far from convinced that sulphonamides given in the commencing stages of acute otitis media (non-perforated) have any value on the course of the infection. The sulphonamides also can have little action where there is erosion of bone.

It may be that with further work on the penicillin group our ideas on the treatment will be revolutionized, but, at present, there is no rule of thumb treatment with the sulphonamide group in an otitis media such as there is in cerebro-spinal meningitis.

My own plan is to give sulphapyridine (M & B 693) if necessary only after the paracentesis has been done—not before—and in fairly large doses. M & B 693 has a stronger action on the pneumococcus though it is more toxic to the patient. This can be continued until the organisms are isolated when the treatment can be changed.

It must be impressed on the student or the general practitioner that if sulphonamide is given in an acute otitis media the ear requires more careful watching than if the drug were not given at all.

Mr. F. W. Watkyn-Thomas said that sulphonamides would act in tissue fluids so long as there was an invasion of the blood-stream, of the lymphatic stream, or of the cerebrospinal system. He did not believe that they would act effectively in bone, or that they could act at all in an abscess when the vessels leading to it were thrombosed. Nor did he think they were effective against pus. For this reason the operative word in Mr. Stirk Adams' paper was the "invasive stage".

He was not altogether in agreement with Mr. Martin about not giving sulphonamides before a paracentesis. He felt that the useful time to give the sulphonamides was, if possible, within the first hour or two of the invasion, and then to give them in a loading dose. Once one did a paracentesis one had pus, and there he would stop the sulphonamides and wait and see what happened.

Some years ago he was an early operator, but now with the sulphonamides they had that confidence which enabled them to await events. If the patient did get meningitis, which was unlikely, a first-rate weapon was available as an aid to surgery. They were fortified in their resolution to wait for a week or a fortnight, and, even without sulphonamides, a great many of these cases did clear up.

Although the number of mastoid cases had certainly fallen it was his impression, although no more than an impression, that the number of intracranial complications had not fallen during the last few years. The mortality of meningitis had enormously improved, but the actual incidence of meningitis had not diminished.

The question of petrositis: When there was any indication of petrosal invasion he was most strongly opposed to giving sulphonamide, which could not affect the process, but could mask the signs, and this was very dangerous. He preferred to keep sulphonamides in reserve and not use them unless he had definite evidence of meningeal or vascular invasion.

Mr. L. Graham Brown desired to stress first the delay in resolution in cases of acute otitis media in which sulphonamides had been given. He would cite one case. A clergyman had an attack and was treated with sulphonamides. The acute condition subsided

and the tympanic membrane healed. Seen for the first time by him it was noticed that the drum head was of a greyish-pink colour, indicating incomplete resolution. Being in a quandary as to what to do, he kept him under observation for a while and then came to the conclusion that it was necessary to incise the drumhead, which he did. That healed again quite readily, but the same appearance persisted for three or four months before the patient regained normal hearing. This case illustrated the delay in resolution which might occur in using sulphonamides. Secondly sulphonamides undoubtedly masked the symptoms and might lull one into a sense of false security. He attended certain municipal hospitals where, after the use of sulphonamides, complications were occasionally seen. One case was that of a girl, aged about 18, who was admitted to hospital with acute otitis. She was treated for a month with sulphonamides in the ordinary way and then discharged. She turned up at the out-patients' department—this was the first time he had seen her—and he diagnosed a mastoiditis and operated at once. Although the lateral sinus was on the point of becoming infected complete recovery ensued.

Another case was not so fortunate. This patient was admitted to hospital and put on treatment with sulphonamides. He did not see the case for a week after admission, and then noticed that the patient complained very little, the temperature was normal, the pulse-rate was normal, and the only symptom was a little deafness with discharge. The appearance of the drumhead did not then suggest a mastoiditis. A week later when he next saw the patient he came to the conclusion at once that mastoidectomy was necessary. He operated and found pus in great quantity in the mastoid. The wound healed completely and the patient left hospital apparently cured. About ten days later he received a telephone message from another hospital to the effect that the same patient had been admitted with signs of meningitis. He died and at autopsy a cerebral abscess was found.

He agreed that sulphonamides were of use in the early stages of infection, but he thought that was their only use apart from their recognized value in intracranial complications. After infection got into the bone no sulphonamides would cure it.

Lieut.-Colonel Norton Canfield, U.S.A.M.C., said that the present paper was very timely. Mr. Stirk Adams had followed his cases through very well. Under circumstances of extremely close clinical observation there could be no doubt that the use of the sulphonamides was very valuable in some cases, but he wished to express agreement with those who had already spoken concerning the difficulties arising from the use of the drug. From their own experience with military personnel they were rapidly coming to the conclusion that the drug was causing more trouble among the troops than it did good. He said that because of the manner in which it had to be used. Military personnel were under much less satisfactory observation in many cases while the drug was being used than were ordinary civilian patients in hospital. These military patients went back to duty and then they had a flare-up of infection. He still thought that in the first few days of infection the drug could be used, but it should be used no longer than one week unless severe complications ensued.

The President said that one point which had not been mentioned was the connexion between the sulphonamides and agranulocytosis. A large number of papers had been published blaming the sulphonamides for these developments. He wrote to the medical department of Messrs. May & Baker, the producers of the drug, and in their reply they said that they were satisfied on the point that sulphonamides could produce agranulocytosis and had done so. Several papers had been published on this point and certain very striking cases were described in the *American Journal of Medical Science* for June 1942, and two other cases in December 1943, which were quoted in *The Practitioner*. These latter patients were cadets aged 22 and 26. Both were critically ill and not expected to recover when sulphadiazine was administered. Most people under these circumstances would have concluded that the sulphadiazine was a factor in the production of the ensuing agranulocytosis, but the surgeon in control of the cases reinstated the sulphadiazine treatment, got the blood level up, and both cases recovered completely under big doses of the compound.

Therefore it did not seem to be proved that the agranulocytosis was due to the sulphonamides. He himself was perfectly convinced, having had one or two cases, that a high septic infection was just as likely to be a factor in the production of agranulocytosis as the sulphonamides. He had a case last year in a child aged 2 with streptococcal infection of the throat. Sulphadiazine was given, the total dose being 2·25 g., a very minute dose. The patient was sent into hospital under the care of one of the physicians. Other treatment for agranulocytosis was carried out, including liver extracts, blood transfusion, pentnucleotide, &c., but the child got worse. He suggested that the child should be put on large doses of sulphathiazole, but the physician in charge would not agree with

that suggestion and the child eventually died. He thought, that in this case, the conclusion that the agranulocytosis was due to a minimal dose of sulphonamides, was quite unfounded. In his opinion the agranulocytosis was a direct result of the extreme septic intoxication. He believed that had it been possible for the child to have been adequately treated with sulphonamides it might have had a fair chance of recovery.

Wing Commander G. H. Bateman gave the Section some statistics concerning the treatment of otitis media in Service hospitals. The cases were all primary ones; recurrent cases had been excluded. During 1942-43 there were 705 cases in this group of which 333 were treated with sulphonamides and 372 without. Among the cases treated with sulphonamides 49, or 14·7%, required mastoid treatment, and in the cases treated without sulphonamides, 35, or 9·5%, required such treatment. These figures might or might not be significant. In the cases treated with sulphonamides the average time from the appearance of the first symptom to the giving of the sulphonamide was 3·4 days and the average time from the first symptom to operation was twenty days. In the cases which did not have sulphonamide the average time from the first symptom to operation was seventeen days. Thus they were very similar groups of cases.

Mr. I. S. Hall said that in Edinburgh during the three years prior to the use of sulphonamides there was an equal number of cases with the same complications as during the last three years—about 32 in each period; this for a hospital population of just over 10,000. These figures went to prove that there was no reduction by the use of sulphonamides in the incidence of complications. But there was possibly an explanation of that circumstance, and if the careful work that Mr. Stirk Adams had told them about was extended they could fairly expect a reduction in the incidence of complications, because the majority of such complications were in recurrent or chronic cases. If the incidence of otitis media and its more serious manifestation of mastoiditis could be reduced in any way, the incidence of complications might eventually be reduced also. From his figures it was shown that whereas the mortality was high among the pre-sulphonamide group, the mortality had been reduced to a quarter after sulphonamides came into use. The important point was that in sulphonamides we had a most potent weapon against the complications of otitis media.

Mr. R. D. Owen said that Mr. Ewart Martin was very fortunate indeed to have had so many cases of acute otitis media with so few complications. His ability to get the cases early and to retain them in hospital under observation from the beginning proved how valuable it was from the very few cases in his series that went on to mastoid retention.

This not only proved the value of early and efficient use of sulphonamides but also that the same consistent result could be obtained by early treatment. This in his opinion was a strong reason why acute otitis media should be made a notifiable disease. It was the only way to prevent the chronic form.

He asked Mr. Stirk Adams whether he advised the use of the Politzer bag during the recovery period following acute otitis media as a measure to prevent the retention of effusion in the tympanum.

Major G. C. Large, R.C.A.M.C., said that during four years of ear, nose, and throat work in the Canadian Army he had yet to do a mastoidectomy. He thought that the main reason was that the cases were received very early, in fact within a few hours. Whether the regimental medical officer had become "ear conscious" he did not know. During the past three months he had been able to work wholly with the British Army; in that time he had seen some 300 ear cases, and had had to do 15 cortical mastoid operations. The cases had been seen an average of five days after onset. The great importance in the use of sulphonamides was the very early treatment with these compounds and in large doses, along with the usual treatment of paracentesis, cleaning and drops.

Mr. R. L. Flett said, with regard to early treatment with sulphonamides, that in a number of these cases of acute otitis media, if one got them within six hours, quite often paracentesis was not required. The drug was then, he thought, definitely of value.

In children under 2 he found this a very treacherous drug to use. He had had three cases in which children between fifteen months and two years of age had been sent into hospital, two of them with a diagnosis of bilateral mastoiditis and one with bilateral otitis media. All were put on sulphonamides, improved and sent home. They were first brought to him about four months later when all three children were totally deaf. He decided to do a mastoid operation on all of them, and the mastoids were found occupied by granulations of a rather pale colour. There was some pus, rather thickish in nature. The mastoids and drums healed up. All these children were now in a deaf and dumb institution. At the early age at which these children had been sent into hospital one could not tell that they had lost their hearing.

Major J. I. Munro Black, R.A.M.C., said that he had been in a hospital where he had seen his acute otitis cases within a matter of hours. Even three days was too late. On seeing the cases within a matter of hours, he was amazed at the satisfactory results with routine treatment using sulphathiazole. He did not extend that treatment for more than two or three days with 15 to 20 g. If at the end of that time they were not doing well he stopped everything. He added that the civilian consultant only saw the patient where the general practitioner failed.

Mr. F. C. Ormerod said that apart from the treatment of complications, the first few hours in the disease were the only time when the sulphonamides were of use. Brigadier Whitby had postulated that the sulphonamides must be given early and in heavy doses, and that they were of no value in the treatment of a bony cavity containing pus.

Figures had been given by Mr. Stirk Adams and Mr. Ewart Martin showing how mastoid operations performed about 1935 compared with 1941-43, but the years up to and including the winter of 1934-35 had severe epidemics of influenza, with a considerable amount of acute otitis media and mastoiditis. In recent years there had been very little influenza, but there had been a severe epidemic in 1943-44. He had had more cases of otitis media and mastoiditis during the past winter than for many years past, and it would be interesting to have Mr. Stirk Adams' and Mr. Ewart Martin's tables continued in order to include the past few months.

Major G. A. Henry, R.C.A.M.C., said that in the winter of 1942-43 in a large camp serving 30,000 to 40,000 men there were some 260 cases of acute otitis media. It was the policy to hospitalize these men at the first sign of an acute middle-ear infection. Sulphathiazole was given in adequate dosage immediately if the drum had not ruptured or paracentesis was not urgently required. If a purulent discharge were already present on admission, unless the patient had a high fever or seemed ill, sulphathiazole was not usually given. Local ear treatment and nasal shrinkage by ephedrine spray was routinely carried out. Among this group only five went on to mastoidectomy. Two of these required extensive operative treatment because of a meningitis which occurred early in the course of the ear infection but fortunately recovered. All cases were hospitalized until the ear had been dry for a few days. He had not noticed that there was much loss of hearing on discharge and only in 1 or 2% of cases was the man sent out with a perforation of the drum.

Major E. P. Fowler, U.S.A.M.C., said that the two openers had spoken about the effect of sulphonamides in the early stages, and Mr. Stirk Adams had given statistics concerning fairly severe cases of otitis media—the two were not comparable. It was extremely important to know what organism was involved, and also to keep in mind the fact that a large number of these cases got well without any sulphonamides at all.

No speaker had mentioned very seriously the question of the development of chronic ear trouble. He was under the impression that in the American Army a certain amount of recurrent ear trouble and eventually chronic ear trouble and permanent deafness were caused by inadequate and promiscuous use of sulphonamides. The sulphonamides were given early by almost all the medical officers, but they were often not given in the right dose and over a long enough period. His own rule of thumb method was to continue until the hearing improved. Sulphadiazine was used in the American Army and it was possible to give it for weeks or even months. The other drugs, sulphapyridine and sulphathiazole, could not be given for such a long period, and they were more likely to cause reactions, especially sulphathiazole. The sensitivity of the individual to the drug must be considered. With some people the drug worked very well, and with others not at all. He had been interested to hear Mr. Ormerod call attention to the increase in mastoiditis this year, because in the American Army they had had the same experience in spite of the almost universal treatment of all acute otitis with sulphonamides.

On the general question he would only say that judgment must be based on the individual case. If the sulphonamides worked, they should be continued for a long time: if they did not cause dramatic improvement at an early stage a mastoidectomy should not be too long delayed. Certainly no drug yet developed permitted one to discard or delay myringotomy as is believed by many general practitioners and pædiatricians.

Mr. Stirk Adams, in reply, stated that he regarded the failure of recovery of hearing in the affected ear as evidence of an unresolved infection and usually an indication for mastoid exploration. Politzerization might be used where incomplete recovery of hearing had taken place, but not in the immediate post-inflammatory period. He stressed the great care required in accepting a recovery as established, and in refusing to allow a patient release from supervision in the phase of apparent recovery, before this recovery had been tested by gradual restoration of physical activity.

INDEX

INDEX

VOL. XXXVII, 1943-4

Note.—In this volume two series of numbers are used for pagination, one being the sectional page number and the other the volume page number. The latter only is used in the Index

INDEX

VOL. XXXVII, 1943-4

Note.—In this volume two series of numbers are used for pagination, one being the sectional page number and the other the volume page number. The latter only is used in the Index

Index